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Supplemental Intravenous Crystalloid Administration Does Not Reduce the Risk of Surgical Wound Infection

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Abstract

Wound perfusion and oxygenation are important determinants of the development of postoperative wound infections. Supplemental fluid administration significantly increases tissue oxygenation in surrogate wounds in the subcutaneous tissue of the upper arm in perioperative surgical patients. We tested the hypothesis that supplemental fluid administration during and after elective colon resections decreases the incidence of postoperative wound infections. Patients undergoing open colon resection

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Implications: Supplemental perioperative intravenous fluid administration did not reduce the rate of wound infection. The apparent lack of benefit may have resulted because hydration's effect on intestinal oxygenation is modest or because the statistical power of our study was limited. Nonetheless, our results suggest that supplemental hydration in the range tested does not impact wound infection rate.

were randomly assigned to small ($n=124$, $8 \text{ mL}\cdot\text{kg}^{-1}\cdot\text{h}^{-1}$) or large volume ($n=129$, $16\text{-}18 \text{ mL}\cdot\text{kg}^{-1}\cdot\text{h}^{-1}$) fluid management. Our major outcomes were two distinct criteria for diagnosis of surgical wound infections: 1) purulent exudate combined with a culture positive for pathogenic bacteria and 2) Center for Disease Control criteria for diagnosis of surgical wound infections. All wound infections diagnosed using either criterion by a blinded observer in the 15 days following surgery were considered in the analysis. Wound healing was evaluated with the ASEPSIS scoring system. Of the patients given small fluid administration, 14 had surgical wound infections; 11 given large fluid therapy had infections, $P=0.46$. ASEPSIS wound healing scores were similar in both groups: 7 ± 16 (small volume) vs. 8 ± 14 (large volume), $P=0.70$. Our results suggest that supplemental hydration in the range tested does not impact wound infection rate.

Keywords

Fluid: Intravenous administration, Balance; Infection: Surgical wound

Introduction

Wound infections are common and serious complications of surgery. For example, there is a 9 to 27% risk of wound infection in patients undergoing colon surgery (1). Surgical wound infections prolong hospitalization by 5 to 20 days (2), increase intensive care unit admissions (3), and substantially increase cost (4).

Wound repair and resistance to infection both depend in part on wound tissue oxygen tension and can potentially be improved by increasing arterial oxygen tension, even of fully saturated blood (3,5). Consistent with this theory, Hopf *et al.* (6) showed that tissue oxygenation better predicts the risk of surgical infection than does the Center for Disease Control (CDC) index. Oxygen is also a critical substrate for tissue repair and wound healing because prolyl and lysyl hydroxylases, and, therefore, collagen synthesis are PO_2 -dependent (7).

Various factors influence tissue oxygenation. For example, mild hypothermia reduces tissue oxygenation (8) and triples the risk of infection (2); conversely, supplemental perioperative oxygen halves the risk of infection by increasing tissue oxygenation (3). However, even supplemental oxygen fails to improve oxygenation in hypoperfused tissues (9). It is thus unsurprising that experimental wound hypoperfusion aggravates infections and reduces scar formation in animals (10,11).

There is considerable evidence that colloid administration titrated to maximize cardiac output reduces complications, including those related to wound healing (12,13,14). However, goal-directed fluid administration is technically difficult, expensive, and somewhat invasive. Adequate vascular volume is thus usually defined by hemodynamic stability and good urinary output. The difficulty with this approach is that hypovolemia reduces peripheral tissue perfusion, as evidenced by decreasing tissue oxygen tension, before reducing blood pressure, increasing heart rate, or reducing urinary output (9).

Guided only by hemodynamic responses, clinicians may inadequately compensate for the enormous fluid losses associated with major surgery. Consistent with this theory, tissue oxygenation is poor in many surgical patients (9) but can be significantly improved by supplemental fluid administration (9,15). We, therefore, tested the hypothesis that doubling the rate of crystalloid fluid administration during and after elective colon resection decreases the incidence of postoperative wound infection.

¹Hopf H. W. Subcutaneous tissue oxygen tension in "well-resuscitated" trauma patients, 1994, Crit Care Med, Vol 22, A60

Methods

The study was conducted with approval from the IRBs at Washington University in St. Louis and the University of Louisville. Written informed consent was obtained from 256 patients aged 18 to 80 years undergoing open elective colon resection with an anticipated duration of surgery greater than two hours. We excluded patients having a recent history of fever or infection, susceptibility to malignant hyperthermia, congestive heart failure, diuretic therapy, any sort of renal failure, or a history of pulmonary edema.

Patients fasted for at least eight hours before surgery. All patients received standard mechanical bowel preparation the night before surgery using standard Fleets phospho soda oral electrolyte solution. In-patients were given IV fluid at a rate of $2 \text{ mL} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$ during bowel preparation and throughout the preoperative evening. A third of the patients were admitted to the hospital on the day of surgery; they performed their bowel preparation at home.

Intraluminal antibiotics were not used. Cefamandole (2 g) and metronidazole (1500 mg) were given IV during induction of anesthesia. Surgeons were encouraged to restrict prophylactic antibiotics to less than 48 hours. Additional antibiotics (*e.g.*, to treat clinically suspected infections) were administered *per* judgment of the attending surgeon.

Anesthesia was induced with IV sodium thiopental (3-5 mg/kg) or propofol (2-4 mg/kg), vecuronium (0.1 mg/kg), and fentanyl (1-3 $\mu\text{g}/\text{kg}$). Anesthesia was maintained with isoflurane in 40% oxygen and 60% nitrous oxide supplemented by fentanyl (1-2 $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$) and vecuronium. Inspiratory oxygen concentrations were adjusted to maintain oxygen saturation $\geq 95\%$. The lungs were mechanically ventilated at a tidal volume of 10 mL/kg at a rate sufficient to maintain end-tidal PCO_2 near 35 mmHg. A bladder catheter was inserted in each patient. Intraoperative distal esophageal temperature was maintained at 36°C using forced-air and IV fluid warming.

After induction of anesthesia and endotracheal intubation, patients were assigned to small or large perioperative hydration using computer-generated randomized codes that were kept in opaque, sealed, sequentially numbered envelopes. Both fluid management schemes were within the range of normal practice and were complemented by replacement of blood loss with crystalloid at a 3:1 ratio. Patients assigned to *small fluid management* were given maintenance of lactated Ringer's solution of 8 to $10 \text{ mL} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$ intraoperatively and for the first postoperative hour. Those assigned to *large fluid management* were given a fluid bolus of 10 mL/kg before induction of anesthesia and subsequently maintained with lactated Ringer's solution at a rate of 16 to $18 \text{ mL} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$ throughout surgery and the first postoperative hour. Additional fluid was given to patients as necessary to maintain urinary output $>1 \text{ mL} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$. Similarly, additional fluid was administered when mean arterial blood pressure decreased to less than 70% of pre-induction value and was unresponsive to minor adjustments in the isoflurane concentration.

Postoperative fluid was given to both groups at a rate of $2 \text{ mL} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$ until the first postoperative morning. Additional fluid was given to patients as necessary to maintain urinary output $>1 \text{ mL} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$. Subsequently, fluid was given at the discretion of the attending surgeon. Plasma expanders (*i.e.*, heta-starch or albumin) were not given.

"Leukocyte filtered" allogeneic blood was administered only as necessary to maintain the prospectively determined target hematocrit that was based on the patient's age and cardiovascular status as previously described (2,3).

Fascial closures were accomplished with running double-stranded monofilament absorbable suture. The skin was closed tightly with staples or absorbable sutures. Throughout surgery,

wound protectors were used. Wound dressing was standardized; pressure dressings were not used.

Postoperative pain relief was maintained with patient-controlled morphine analgesia (2 mg bolus, 6-minute lockout). Prophylactic antiemetics were not given, as per standard of care. Postoperative nausea and vomiting were treated with ondansetron (4 mg IV). Additional doses were given as necessary by clinicians blinded to group assignment. During recovery, patients were given supplemental oxygen via nasal prongs at a rate of 2 L/min; additional oxygen was given as necessary to maintain oxygen saturation $\geq 95\%$.

After one hour of recovery, the anesthesia record and perioperative fluid administration records were sealed in an envelope marked: "Anesthesia Record. Do not open unless necessary for clinical care until date (16 days after surgery)." Thus, the surgeons and investigators evaluating wound infections and healing were unable to determine group assignment or perioperative fluid management from patient records.

Appropriate clinical characteristics of each treatment group were tabulated. Preoperative laboratory values and historical factors likely to influence wound healing or resistance to infection were recorded; they included smoking history, preoperative hemoglobin concentration, co-existing systemic diseases, and drug therapy.

Anesthetic and hemodynamic data, as well as core temperatures and forearm minus fingertip skin-temperature gradients, were measured throughout the treatment period in 15-minute intervals.

Preoperative risk of infection was evaluated using the Center for Disease Control (CDC) Study on the Efficacy of Nosocomial Infection Control (SENIC) score, where one point each was assigned for ≥ 3 diagnoses, surgical duration ≥ 2 hours, abdominal site of surgery, and the presence of a contaminated or dirty-infected wound (16). Infection risk was further quantified using the National Nosocomial Infection Surveillance System (NNISS), in which risk was predicted based on type of surgery, ASA Physical Status rating, and surgical duration (17). Our primary outcome measure was the incidence of postoperative wound infection. Surgical wounds were evaluated daily by a physician blinded to group assignment. After discharge, the same-blinded physician evaluated patients during their two-week clinic visits. Patients not returning to the clinic were contacted by phone by an investigator blinded to group assignment and treatment. All wound infections diagnosed in the 15 days following surgery were considered in the data analysis. We restricted the diagnostic interval to 15 days because no infections were detected between 16 and 30 days in our previous study in this surgical population (2).

Our major outcome was either of two distinct criteria for diagnosis of surgical wound infections. The first, as in our previous studies (2,3) was purulent exudate and a positive culture. The second was the 1992 revision (18) of the CDC criteria for surgical wounds (16) with the exception that we restricted our diagnostic period to 15 rather than 30 days.

Wound healing and infections were numerically scored using the ASEPSIS system (19). This is an established and validated system for quantifying surgical wound infections and evaluating wound healing.

Subcutaneous oxygen tension (P_{sqO_2}) in the upper arm was evaluated in a subgroup of 56 patients with a polarographic Clark-type tissue oxygen sensor (Licor, Inc., Germany). As the hypothesis of our outcome study was based on the results of this preliminary study, tissue oxygenation in these patients was reported previously (15). However, randomization and follow-up of this subgroup was properly performed within current the outcome study.

We recorded the incidence of nausea and vomiting and anti-emetic use in each group, during recovery and on the first postoperative day. The severity of nausea was evaluated after one postoperative hour with a 100-mm visual analog scale (0 mm = no nausea; 100 mm = worse possible nausea). Postoperative pain was evaluated with a 100-mm visual analog scale at 30-minute intervals during the first hour of recovery and again after 24 hours (0 mm = no pain; 100 mm = worse possible pain).

Attending surgeons, who were unaware of the patient's group assignment, made the decision to discharge the patient from the hospital. Discharge was based on routine surgical considerations, including return of bowel function, control of infections (if any), and adequate healing of the incision.

Based on previous studies (3), we anticipated that the incidence of surgical wound infections without and with supplemental fluid administration would be 11 and 5%, respectively, in patients maintained at a core temperature of 36°C and with 30% oxygen administration. Our original study design thus called for a total of 750 participants. The prospective criterion for ending the study after 250 patients was a difference in the incidence of surgical wound infection with a two-tailed P value < 0.0125 . After 500 patients, the study was to be stopped if $P < 0.0161$. To compensate for the two initial analyses, a P value of 0.0356 was to be required upon completion of all 750 patients. To avoid a Type I statistical error resulting from multiple comparisons, infection incidence was the sole criterion for stopping the study early (20).

The number of postoperative wound infections and all other categorical outcomes in each volume group were compared using a Chi Square test with Yates correction for continuity. Additionally, multivariable logistic regression was used to examine the relationship of surgical wound infection rate and fluid management while controlling for potential confounding factors. Wound healing scores and other ordinal variables were compared with Mann-Whitney rank-sum test. Days of hospitalization and other continuous variables were compared with unpaired, two-tailed t -tests.

Results

An initial data analysis was performed as planned after 250 patients. However, an additional 6 patients were enrolled while the analysis was being conducted. These patients were included in the analysis, which was thus based on 256 patients; of these, 253 completed the trial (Fig. 1)

Based on the results in the initial 253 patients, we performed two sample-size calculations. The first indicated that approximately 750 patients would be required to provide an 80% power for excluding a two-fold difference in infection rates in each volume group. The second indicated that more than 4100 patients would be required to have an 80% power to identify a statistically significant difference between the treatments. The Data Safety Monitoring Board thus concluded that the hypothesis was unlikely to be confirmed even with a very large number of patients; they also concluded that the apparent effect of supplemental fluid administration (if any) was likely to be clinically unimportant compared to other interventions. The study was thus stopped.

Demographic and morphometric characteristics were similar in patients assigned to small volume ($n=124$) and large volume ($n=129$) fluid management. Potential confounding factors were also similar. SENIC and NNIS scores were virtually identical in the two treatment groups (Table 1); anesthetic and surgical management were also similar (Table 2).

Large volume patients received perioperatively almost twice as much total fluid as the small volume patients (5.7 ± 2 L versus 3.1 ± 1.5 L) (Tabl.2). Among the 253 patients, there were

14 infections in patients assigned to small fluid management and 11 in those assigned to large fluid management ($P = 0.462$).

The overall infection rate was 9.9%, which was high compared to the 4.2% rate predicted by the NNIS score. ASEPIS wound healing scores were similar in the two volume groups, as were the times at which solid food was tolerated (Table 3). Four of 13 wound cultures failed to grow pathogenic bacteria. The overall infection rate at the University of Louisville was 14%, whereas it was 9% at Washington University ($P = 0.48$). Wound infection rates did not differ significantly between patients admitted the morning of surgery (11.9%) and patients who were admitted the night before surgery and, therefore, had IV hydration during mechanical bowel preparation (7.7%; $P = 0.281$).

Although preoperative co-morbidities did not differ, preoperative hemoglobin concentrations were less in patients who developed infections (11.2 ± 1.7 vs. 12.2 ± 1.9 g/dL, $P = 0.01$).

Including hemoglobin concentration, inpatient vs. outpatient hydration, co-morbidities, and other potential confounding factors in a multivariate analysis confirmed that volume management did not influence infection rate.

Eleven patients were admitted to the ICU, 3 in the small volume group versus 8 in the large volume group, $P = 0.14$ (Table 3). None of the patients died. The duration of hospitalization was virtually identical in the small and large fluid management groups. However, the duration of hospitalization was 13.9 ± 10.0 days in the infected patients, whereas it was 6.4 ± 3.0 days in the uninfected patients ($P < 0.001$).

About a quarter of the patients experienced postoperative nausea during the initial 24 postoperative hours. There was no difference in the incidence of nausea or vomiting in the two volume groups, either in the first hour or during the first 24 hours (Table 4).

Discussion

Infection rates did not differ significantly in the patients assigned to small (11.3%) or large (8.5%) fluid management. This finding was surprising since our previous study suggested that aggressive fluid management should decrease infection rate. There are, however, at least three possible reasons why we were unable to reduce infection rate even though supplemental fluid increases subcutaneous oxygen tension (15). The first is that although aggressive fluid management increases subcutaneous tissue oxygenation by ≈ 15 mmHg (15) and previous work suggests that a 15-mmHg improvement in tissue oxygenation is likely to reduce infection risk (6), this increase is small compared with providing supplemental inspired oxygen, which doubles tissue oxygenation from ≈ 60 to ≈ 110 mmHg (3).

The second factor is that in our previous study we measured tissue oxygen partial pressure in a surrogate wound in the upper arm rather than adjacent to the abdominal wound or in the intestines *per se*. Oxygenation at the arm, wound, and colon are similarly improved by supplemental inspired oxygen (21-23). However, supplemental fluid administration, specifically crystalloids, might affect tissue oxygenation differently in injured and uninjured tissue. Thus, in this specific case a surrogate wound on the arm might not reflect perfusion and oxygenation of the actual wound. It is a major limitation of our study that we did not evaluate wound tissue oxygen tension. Furthermore, recent data — which were unavailable at the time of our study — suggest that intestinal oxygenation in swine is minimally influenced by hydration (24). Hydration strategies, at least in the range tested, thus appear to have less effect on intestinal oxygenation than other proven methods of reducing infection risk such as supplemental oxygen administration (24).

The third factor is that our current results provide only a 37% power for detecting a factor-of-two treatment effect. It thus remains possible that supplemental hydration does reduce infection risk. Although our results thus suggest that the effects of hydration are small in our general surgical patient population, in some specific high-risk patient populations any decrease of wound infection rate might be important.

It is important to recognize that even our small volume group was given adequate fluid and was not hypovolemic by any routine clinical criteria. For example, mean arterial blood pressure and heart rate were virtually identical in the two groups. That supplemental fluid administration did not reduce infection risk is by no means an indication that hypovolemia is harmless. In fact, hypovolemia reduces healing of colonic anastomoses (25).

Our primary result was that the risk of surgical wound infection was similar in patients given 3.1 versus 5.7 L of crystalloid perioperatively; bowel function and duration of hospitalization were also similar in the two treatment groups. This result contrasts with those of Brandstrup *et al.* (26) who found that fluid restriction (with the goal of maintaining an unchanged body weight) reduced the risk of complications in patients undergoing colon resection. They also differ from Holte *et al.* (27) who reported that a fixed regimen of 3,000 mL versus 500 mL of crystalloid for elective laparoscopic cholecystectomy improved outcome.

Additionally, numerous studies report that Doppler-directed colloid administration improves recovery characteristics and shortens hospitalization. For example, Gan *et al.* (12) found that goal-directed colloid administration reduced the risk of complications, sped return of bowel function, and shortened hospitalization in patients undergoing major surgery with anticipated blood loss exceeding 500 mL. Mythen and Webb (13) reported that Doppler-directed colloid administration improved gut mucosal perfusion (as determined by gastric tonometry), reduced the risk of complications, and shortened hospitalization in cardiac surgery patients. And finally, Sinclair *et al.* (14) similarly reported that goal-directed colloid administration improved recovery characteristics and shortened hospitalization in patients undergoing hip fracture repair.

Taken together, available literature indicates that goal-directed colloid administration improves outcomes, especially shortening the duration of hospitalization. Fixed volume regimens, in contrast, are variously reported as being detrimental, neutral, or beneficial. It thus seems likely that variability among patients precludes selecting a fixed mL.kg⁻¹.h⁻¹ fluid regimen that will optimally serve most patients, even within a particular type of surgery. We also note that study designs concerning types and amounts of fluids and primary outcomes in the major studies often differed widely. Furthermore, fluid regimens that are optimal for one organ or system may well prove detrimental to another. Results of vascular volume studies must thus be interpreted in light of the type of fluid, management strategy, patient population, and specific outcomes.

We (28) and others (29) have shown that supplemental perioperative fluid administration reduces the risk of postoperative nausea and vomiting. For example, patients given a loading dose of 15 mL/kg crystalloid experienced less nausea and vomiting after gynecologic surgery than those given 2 mL/kg (28). However, the incidence of nausea and vomiting during the first 24 hours after surgery was similar in our current treatment groups. This is consistent with other studies in which a benefit of supplemental fluid administration was not apparent (30,31).

Our overall infection rate was roughly twice that predicted by the NNIS score (17). In this respect, the current results are similar to our previous ones (2,3). It is likely that our infection rate was relatively high in part because the studies were primarily conducted in tertiary referral hospitals that cater to relatively sick patients who often suffer serious underlying conditions. We also included patients at high risk of infection including those taking immunosuppressant

medications. And finally, it is worth noting that the NNISS data set is limited by being based on self-reports by surgeons, whereas wounds in our studies are evaluated daily by trained physicians using two sets of strict diagnostic criteria. However, our observed infection rate is still lower than in most recent studies, which report infection rates in similar patient populations above 15% (26,32). Our patient population was diverse, but no more so than in all the other studies mentioned. We performed a multi-variant analysis to evaluate the potential contribution of coexisting diseases and found that there was no evidence that pre-existing patient factors contributed substantially to our results or would alter our conclusions. Our infected patients remained in the hospital a full week longer than uninfected patients, suggesting that our diagnostic criteria were appropriate and that our infections were indeed clinically important.

Approximately 5% of our patients were admitted to the ICU, twice as many in the large volume group as compared to the small volume. One 63-year-old female patient (ASA II with no cardiac history) from the large volume group was admitted to the intensive care unit because she developed pulmonary edema. Treatment was conservative without any ventilatory support, and she was discharged from the ICU the next day. She had no further complications and was discharged from hospital on day 8. Three patients, all in the large volume group, were admitted due to surgical site infection. Two of them developed deep infection and sepsis. Other reasons for ICU admission were myocardial infarction (large volume group), atrial arrhythmia (large volume group), postoperative psychoses (both groups) or due to surgical complications. However, ICU admissions were not our primary outcome and thus we neither can draw any conclusions about the association of group assignments and ICU admission nor about fluid management and the different complications leading to these admissions.

Our patients were all anesthetized with nitrous oxide, and although there are many advantages to nitrous oxide, its use precludes simultaneous administration of supplemental oxygen. Although we have demonstrated that supplemental oxygen halves infection risk (3), a recent smaller study by Pryor *et al.* (32) concluded just the opposite. Furthermore, the administration of 80% oxygen was not standard of care at the time when we performed this study and, in fact, is still not as of the writing of this article. Infection rates may have been less had we substituted supplemental oxygen for nitrous oxide. However, it seems unlikely that doing so would alter our overall conclusion that supplemental fluid administration does not reduce infection risk.

In summary, infection rates were similar in patients given small fluid replacement (≈ 3.100 mL) and in those given large fluid replacement (≈ 5.700 mL). The apparent lack of benefit from supplemental fluid may have resulted because the effect of hydration on intestinal oxygenation is modest or because the statistical power of our study was limited. Nonetheless, our results suggest that supplemental hydration in the range tested does not have a major impact on wound infection risk.

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Fig. 1. Trial profile. “Withdrawn” includes patients who withdrew consent at any point during the follow-up period.

Table 1.

Patient Characteristics.

		Small Volume N = 124	Large volume N = 129	P
Sex (M/F)		60 / 64	65 / 64	0.750
Weight (kg)		77 ± 18	78 ± 17	0.689
Age (years)		53 ± 14	52 ± 15	0.859
ASA status (I/II/III)		13 / 81 / 17*	9 / 86 / 18*	0.642
Smoker (Y/N)		25 / 99	25 / 104	0.876
Diagnosis (%)				0.684
	Cancer	61%	62%	
	Inflammatory bowel disease	30%	32%	
	Other	9%	6%	
Operative site (%)				0.394
	Colon	65%	70%	
	Rectum	35%	30%	
Hemoglobin (g/dL)		12.0 ± 1.8	12.5 ± 2.1	0.424
Study Site (St. Louis / Louisville)		97 / 27	106 / 23	0.431
Bowel Preparation (inpatient / outpatient)		78 / 46*	84 / 45*	0.814
SENIC score 1/2/3 (#)		49 / 70 / 5	39 / 86 / 4	0.248
NNISS score 1/2/3 (#)		68 / 34 / 7*	64 / 42 / 5*	0.528
Infection rate predicted by NNISS (%)		4.2	4.2	—

* Some data from these categories were missing. SENIC is the Center for Disease Control Study on the Efficacy of Nosocomial Infection Control. NNISS is the National Nosocomial Infection Surveillance System score.

Table 2.

Perioperative Management.

	Small Volume N = 124	Large Volume N = 129	P
Preoperative Crystalloid (L)		0.7 ± 0.3	
INTRAOPERATIVE DATA			
Fentanyl (µg)	196 ± 156	199 ± 133	0.866
Isoflurane (%)	0.9 ± 0.2	0.9 ± 0.2	0.452
Mean Arterial Blood Pressure (mmHg)	81 ± 10	81 ± 9	0.876
Heart rate (bpm)	80 ± 12	80 ± 13	0.745
Crystalloid (L)	2.5 ± 1.3	3.9 ± 1.9	<0.001
Urine output (mL)	310 ± 276	490 ± 393	<0.001
Estimated blood loss (mL)	333 ± 349	322 ± 331	0.796
Red-cell transfusion			
	Patients (number)	9	0.312
	Total units (number)	22	---
Duration of surgery (h)	2.6 ± 1.1	2.6 ± 1.0	0.909
Core temperature (°C)	35.9 ± 0.5	35.9 ± 0.6	0.720
FiO ₂ (%)	45.8 ± 14.5	43.3 ± 10.3	0.123
Arterial oxygen saturation (%)	98.9 ± 1.1	99.0 ± 1.1	0.556
End-tidal PCO ₂ (mmHg)	32.5 ± 2.9	32.0 ± 2.7	0.152
Skin-Temperature Gradient (°C)	0.5 ± 1.4	0.5 ± 1.3	0.972
POSTOPERATIVE DATA			
Crystalloid (L)	0.6 ± 0.3	1.1 ± 0.4	<0.001
Oxygen saturation (%)	98.4 ± 3.2	97.8 ± 3.3	0.099
VAS	39.9 ± 26.3	39.5 ± 28.3	0.911

VAS is visual analog pain scores. Postoperative results were obtained during the first hour of recovery. Skin-temperature gradient is calculated as forearm temperature minus fingertip temperature; values exceeding 0°C indicate vasoconstriction.

Table 3.**Principal Results.**

	Small Volume	Large Volume	P
Infection Diagnosed by Pus and a Positive Culture (%)	5.7	4.7	0.720
Infection Diagnosed by CDC Criteria (%)			
Superficial	6.5	3.9	0.354
Deep	5.7	5.4	0.939
Peritoneal	0.0	2.3	0.247
Any CDC infection	10.5	7.0	0.322
Total Infection by Either Criterion (%)	11.3	8.5	0.462
ASEPSIS score	8 ± 14	7 ± 16	0.698
Intensive Care Admission (%)	2.4	6.2	0.140
First solid food (postoperative days)	4.2 ± 1.9	4.4 ± 2.7	0.448
Duration of hospitalization (days)	7.3 ± 4.0	7.0 ± 5.4	0.701

CDC is Center for Disease Control. ASEPSIS is a wound-healing score (19). Infections as diagnosed by pus and a positive culture and by CDC criteria are not mutually exclusive. Consequently, the total infection column is not the sum of each infection type.

Table 4.
Postoperative Nausea and Vomiting.

	Small Volume	Large Volume	P
One hour after surgery (N=253)			
Nausea (%)	12.1	12.4	0.941
Vomiting (%)	0.8	0.0	1.00
Rescue Ondansetron (%)	8.9	5.4	0.287
0-24 hours after surgery (N=203)*			
Nausea (%)	24.7	28.3	0.566
Vomiting (%)	4.1	2.8	0.614
Rescue Ondansetron (%)	18.6	16.0	0.635

* Data collected at St. Louis site only.