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Perioperative fluid status and surgical outcomes in patients undergoing cytoreductive surgery for advanced epithelial ovarian cancer

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HIGHLIGHTS

- Positive fluid status is common after cytoreductive surgery for advanced epithelial ovarian cancer.
- Positive fluid status after cytoreductive surgery is associated with surgical site infections.
- Fluid management is a key component of interventions to prevent surgical site infections.

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ABSTRACT

Objective. The objective of this study is to investigate the impact of fluid status on perioperative outcomes of patients undergoing cytoreductive surgery (CRS) for advanced epithelial ovarian cancer (EOC).

Methods. Patients undergoing CRS for stage III or IV EOC at a comprehensive cancer center from 12/2010 to 05/2015 were identified. Those who underwent upper abdominal procedures or colon resections were included. Demographic, perioperative, and 30-day complication data were collected. Perioperative weight change was utilized as a surrogate for fluid status. The time to diuresis (tD) was defined as the postoperative day the patient's weight began to downtrend.

Results. One hundred ten patients were included. Median age was 62 years and median BMI 25.8 kg/m^2. The majority (74.5%) were stage IIIC. At least 1 bowel resection was performed in 60 cases (54.5%). A median of 5381 mL of crystalloid (range 1000–17,550 mL) and 500 mL of colloids (range 0–2783 mL) was given intraoperatively. The median perioperative weight change was +7.3 kg (range − 0.9 kg to +35.7 kg). The median tD was 3 days (range 1–17 days). On univariate analysis, net positive fluid status was associated with unscheduled reoperation, anastomotic leak, surgical site infections (SSI), and length of stay >5 days. On multivariate analysis, fluid status was independently associated with SSI ($p = 0.01$).

Conclusions. Perioperative fluid excess is common in patients undergoing CRS for EOC and is independently associated with SSI.

1. Background

The goal of cytoreductive surgery (CRS) in advanced ovarian cancer is complete surgical resection to no gross residual disease. Each incremental decrease in the volume of residual disease after CRS has been associated with progressively improved overall survival [1–2]. To achieve this goal, multi-organ resections including extensive pelvic dissection, intestinal resection, and upper abdominal procedures are commonly required [3]. While radical CRS may be associated with morbidity and prolonged recovery, radical procedures are associated with improved survival outcomes when compared to less radical or suboptimal cytoreduction [4–6].

Meticulous perioperative care is critical to optimize outcomes for women undergoing radical CRS for advanced ovarian cancer. A key aspect of perioperative care is fluid management. In a study of 71 patients undergoing colorectal procedures, 17% had postoperative complications attributable to fluid management [7]. Inadequate fluid resuscitation can

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result in organ hypoperfusion and damage, while excessive fluid administration may lead to delayed time to extubation, tissue edema, organ dysfunction, delayed wound healing, and prolonged hospital stays [8, 9]. In the general surgery literature, perioperative weight gain has been utilized as a surrogate for fluid excess; an increase of 3 kg or more can result in increased morbidity and longer length of stay [9, 10]. Lowell et al. noted a significant increase in mortality from 10.3% to 31.6% in patients who gained <10% of their body weight compared to those who gained >10% of their body weight in the postoperative period [11].

CRS for advanced ovarian cancer requires a particularly delicate fluid balance. The operations are lengthy and often involve multiple organ systems. Procedures such as stripping the diaphragm or removing peritoneal implants disrupt cell layers and leave exposed surfaces that are prone to fluid loss. Importantly, these patients are prone to production of massive ascites and possess a poor nutritional status. Collectively, these factors contribute to large perioperative fluid shifts, which have important implications related to perioperative morbidity and postoperative fluid management. Despite its importance, the impact of fluid disruptions on perioperative morbidity in women undergoing CRS for advanced ovarian cancer has not been well studied. The study objective was to describe perioperative fluid status, and its association with morbidity, in this cancer cohort.

2. Methods

After obtaining Institutional Review Board approval, all women who underwent surgery for ovarian, fallopian tube, or peritoneal cancer between 12/2010 and 05/2015 at the Johns Hopkins Hospital were identified using an institutional ovarian cancer registry database. All patients were operated on by experienced gynecologic oncologic surgeons trained in radical upper abdominal and pelvic cytoreductive surgical techniques. Standard antibiotic prophylaxis was administered within 30 min of skin incision according to Centers for Disease Control and Prevention (CDC) guidelines [12]. Antibiotics were appropriately re-dosed intraoperatively based on time elapsed and blood loss. Only those with stage III or IV disease who underwent an exploratory laparotomy, resection of the internal gynecologic viscera if present (ovaries, fallopian tubes, and uterus), and one additional procedure (small or large bowel resection, omentectomy for omental cake, splenectomy, diaphragm or peritoneal stripping, liver resection, distal pancreatectomy and/or cholecystectomy) were included in the study. Patients were excluded if they did not have data on perioperative fluid status and weight measurements, had a pathologic diagnosis of non-epithelial ovarian cancer or were pregnant.

Relevant clinical data were abstracted from both the inpatient and outpatient electronic medical records. Demographic, perioperative, and 30-day perioperative complication data were collected. “Length of stay” was calculated starting on postoperative day 0. Perioperative weight change, defined as the difference between preoperative weight and the maximum weight measured during the postoperative period, was used as a surrogate for fluid status. Fluid excess was defined as perioperative weight gain. Preoperative weights were obtained from the last clinic visit prior to the operation. The “time to diuresis” was defined as the postoperative day the patient's weight began to downtrend. Perioperative complications included unscheduled ICU admission, unscheduled reoperation, hospital readmission, venous thromboembolism, anastomotic leak, surgical site infection (SSI), pelvic abscess, small bowel obstruction, ileus, pulmonary complications, and mortality. SSI is defined as an infection related to an operative procedure that occurs at or near the surgical incision, which includes both superficial and deep incisional infections, within 30 days of the procedure [11]. Pulmonary complications included effusion, pneumonia, and pneumothorax.

The presence or absence of significant associations between weight change, which was analyzed as a continuous variable, and each of the 30-day postoperative complications were investigated. Fischer's exact test and simple logistic regression were utilized for univariate analysis. Multivariate logistic regression was subsequently employed to determine if significant relationships were maintained. A multivariate logistic regression model was employed for each outcome and controlled for known poor prognostic risk factors including age, BMI, stage, presence of ascites, preoperative albumin, operative time, and estimated blood loss. SPSS Version 22.0 (IBM Corp, Armonk, NY) was used for statistical calculations with significance set at 0.05 and power at 80%.

3. Results

In total, 110 women underwent surgery for stage III or IV ovarian, fallopian tube, or peritoneal cancer met inclusion criteria. Demographic information is detailed in Table 1. The median patient age was 62 years (range 31–88 years). The median BMI was 25.8 kg/m^2 (range 16.6–47.9 kg/m^2). The most common comorbidity observed was hypertension (43.6%). Performance status was not available for most patients and, therefore, not included. Stage distributions were as follows: 11 (10.0%) stage IIIA–B; 82 (74.5%) stage IIIC; 14 (12.7%) stage IV. Ascites, identified through both the anesthesia record and operative notes, was present preoperatively in 47 patients (42.7%).

Surgical and perioperative data is listed in Table 2. Residual disease of less than or equal to 10 mm was achieved in 104 (94.5%) of patients. At least one bowel resection was performed in 60 cases (54.5%). The median operative time was 331 min (range 140–755 min). The median estimated blood loss was 750 cm^3 (mL; range 50–5000 mL). The median volume of crystalloid infused intraoperatively was 5381 mL (range 1000–17,550 mL) and within the first 48 h postoperatively was 6433 mL (range 1600–20,246 mL). The median volume of colloids infused intraoperatively was 500 mL (range 0–2783 mL) and within the first 48 h postoperatively was 0 mL (range 0–3100 mL). Of 110 patients, 49 (44.1%) received packed red blood cell transfusions intraoperatively. The mean number of units transfused was 1.3. The median perioperative weight change was +7.3 kg (range −0.9 to +35.7 kg). Only one patient had weight loss during their hospitalization. The median time to diuresis was 3 days (range 0–17 days).

There were no deaths within 30 days of surgery. Fifty-six cases (50.5%) required intensive care unit (ICU) admission. Of those, the vast majority of patients were scheduled admissions directly from the OR with only 3 patients (2.7%) transferred postoperatively from the surgical floor. Thirteen patients (11.7%) required unscheduled reoperation and 16 patients (14.4%) were readmitted. Pulmonary complications, including pulmonary edema, effusion, pneumothorax, or pneumonia were the most common adverse events observed within 30 days postoperatively (20.7%), followed by surgical site infection (SSI) (19.8%). Table 3 outlines further details regarding postoperative complications. On univariate analysis, perioperative weight gain was significantly associated with unscheduled reoperation, anastomotic leak, SSI, and length

Table 1
Patient demographics and surgical variables.

Variable	Whole cohort N (%)
Age (years)	
Median (range)	62.0 (31–88)
Body mass index (kg/m^2)	
Median (range)	25.8 (16.6–47.9)
Medical comorbidities	
Hypertension	48 (43.6%)
Diabetes mellitus	14 (12.7%)
FIGO Stage	
IIIA–B	11 (10.0%)
IIIC	82 (74.5%)
IV	14 (12.7%)
Presence of ascites	47 (42.7%)
Preoperative albumin	
Mean (SD)	4.15 (0.58)