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Original research

Ratio of intra-operative fluid to anesthesia time and its impact on short term perioperative outcomes following gastrectomy for cancer: A retrospective cohort study

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HIGHLIGHTS

- Evaluates the short-term impact of intra-operative fluid administration during gastrectomy for cancer.
- Utilizes multi-institutional database.
- Fluid resuscitation <10 ml total fluid per minute is associated with an increased risk of complications.

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ABSTRACT

Background: This study evaluates the short-term impact of fluid administration during gastrectomy for cancer.
Methods: A multi-institutional database of patients undergoing gastrectomy for cancer from three tertiary centers was reviewed. Logistic and linear regression analyses were performed.
Results: 205 patients were included. The majority of patients ($n = 116$, 57%) underwent proximal or total gastrectomy. Median anesthesia time was 280 min (range 95–691 min). Median intraoperative crystalloid administration was 2901 ml (range 500–10,700 ml). Median colloid administration was 0 (range 0–3835 ml), although only 66 patients (32%) received colloid. On multivariate analysis, patients who received <10.0 ml total fluid per minute of anesthesia had a significantly higher risk of complications (OR 4.12, $p = 0.010$). Crystalloid and total fluid administration ratios did not significantly affect LOS or discharge disposition.
Conclusions: Restricting intra-operative fluid resuscitation to <10 ml total fluid per minute anesthesia is associated with an increased risk of complications in patients undergoing gastrectomy for cancer.

1. Introduction

Intraoperative fluid resuscitation with a large positive fluid balance has been shown in recent years to correlate with postoperative morbidity and mortality [1]. A liberal resuscitation approach is increasingly being abandoned in favor of goal directed therapy in an effort to maintain tissue perfusion using a minimum amount of crystalloid infusion [2]. This concept opposes the prevalent theory that patients are often hypovolemic upon presentation and that third-space fluid losses must be counterbalanced [2]. In addition to fewer complications such as anastomotic leak or sepsis, patients undergoing intra-abdominal surgery resuscitated using goal directed therapy may also recover faster, with shorter lengths of hospital stay (LOS) [3,4].

Gastric cancer, while relatively uncommon in the United States, is the fifth most common malignancy in the world, with nearly half

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of cases occurring in Eastern Asia [5]. Although the overall incidence in the United States is decreasing, gastric cancer still accounts for over 24,000 new cases per year based on the National Cancer Institute's Surveillance, Epidemiology, and End Results Program [6]. A single institution experience from Memorial Sloan-Kettering Cancer Center showed a complication rate of 62% following total gastrectomy, with 28% of patients experiencing a major adverse event requiring invasive intervention, of which anastomotic leak was the most common [7]. The US Gastric Cancer Collaborative reported a 43% overall complication rate for all included curative-intent gastrectomies, of which 42% were a Clavien-Dindo grade III or higher [8].

Restricted intraoperative fluid, with goal directed therapy based on minimally invasive hemodynamic monitoring, has been associated with improved outcomes in complex abdominal surgeries such as pancreaticoduodenectomy and esophagectomy [9,10]. This study aimed to evaluate the impact of intraoperative fluid administration on perioperative outcomes in a cohort of patients undergoing curative intent gastrectomy for cancer.

2. Methods

2.1. Data

This is a retrospective cohort study based on data acquired from electronic medical records that included patients undergoing gastrectomy for cancer between 1997 and 2014. Patients from three tertiary referral centers were included: Herbert Irving Comprehensive Cancer Center at Columbia Medical Center, Penn State Hershey Medical Center, and Moffitt Cancer Center and Research Institute. Multiple surgeons performed all of the operations over the time period. There was no standardized protocol for anesthetic replacement of fluid, either crystalloid or colloid, or blood transfusion.

Patient level variables were collected including demographics (age, gender, and race/ethnicity), body mass index (BMI), cigarette and alcohol use, ASA class, type of surgery (proximal and total gastrectomy or distal gastrectomy), estimated blood loss (EBL), blood transfusion, pathologic factors (perineural and lymphovascular invasion, margin status), and administration of neoadjuvant chemotherapy. The volume of total fluid per minute of anesthesia time, or intra-operative total fluid ratio (TFR), was determined by dividing the sum of the volume of intra-operative crystalloid and colloid administered in milliliters by the recorded number of minutes of anesthesia time (ml/min). Based on a sensitivity analysis that demonstrated a significant difference in outcomes when TFR was $\geq$10 ml/min, patients were divided into two groups: patients with a TFR <10.0 ml/min and patients with a TFR $\geq$10.0 ml/min. Blood products transfused were not included in the total fluid ratio and were treated as a separate covariate.

Intra-operative crystalloid ratio (CR) was determined by dividing the total volume of intra-operative crystalloid in milliliters by the recorded number of minutes of anesthesia time (ml/min). Patients were divided into four groups based on the 25th, 50th, and 75th percentiles: patients with a CR $\leq$ 9.0 ml/min, patients with a CR 9.0–11.0 ml/min, patients with a CR 11.1–14.0 ml/min, and patients with a CR > 14.0 ml/min.

Three outcomes were studied: any post-operative complication, LOS, and discharge disposition. Severity of complications was determined using the Clavien-Dindo classification system [11]. LOS was measured as the total length of admission to the hospital where the gastrectomy was performed. Discharge disposition was classified as discharge to home, rehabilitation facility, facility other than a rehabilitation facility (nursing home or prison), skilled nursing facility or death. This work was completed in full compliance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines [12].

2.2. Statistical analysis

Statistical analysis was performed primarily to determine whether intra-operative fluid administration ratios were significantly associated with outcomes after controlling for important covariates. Univariate analysis using χ^2 tests for binary and categorical variables was performed to determine whether there were differences in patient characteristics across fluid ratio groups. Logistic regression was used to model the effects of intra-operative fluid ratio on complications and discharge disposition after controlling for patient and procedure characteristics. LOS was fit to a generalized linear regression model assuming a gamma family of distributions and log link function. These models were chosen because LOS data were highly skewed and did not meet the normality assumption of the classical linear model. We report the marginal effects from the generalized linear models, which show the effect of a one-unit change in the independent variable on the outcome. All statistical analyses were performed using STATA (version 12.1, StataCorp LLP, College Station, TX). Statistical significance for all analyses was defined as a P-value < 0.05.

3. Results

3.1. Patient characteristics

There were 205 patients who underwent gastrectomy for cancer between 1997 and 2014 from the three tertiary referral centers. The median age was 67.2 years, with a slight male predominance (n = 111, 54%). Sixty-three percent (n = 130) of the cohort was overweight or obese (BMI $\geq$ 25). The median ASA class was 3. The majority of patients (n = 116, 57%) underwent proximal or total gastrectomy. Median anesthesia time was 280 min (range 95–691 min). Median intraoperative crystalloid administration was 2901 ml (range 500–10,700 ml). Median colloid administration was 0 (range 0–3835 ml), although only 66 patients (32%) received colloid. Fifty-six patients (27%) had a post-operative complication, including six patients (3%) who had an anastomotic leak and six patients (3%) who had a severe pulmonary complication.

Patients were stratified by TFR with a median of 12.2 ml/min. Fifty-nine (29%) patients had a TFR < 10.0 ml/min and 146 (71%) patients had a TFR $\geq$ 10.0 ml/min. Demographic characteristics are shown in Table 1. There was no significant difference between groups in most characteristics, with the exception of EBL and transfusion requirement. As EBL increased, a greater percentage of patients received $\geq$10.0 ml of total fluid per minute (p = 0.001). A total of 32 (16%) received intraoperative blood transfusion, 4 (7%) in the TFR < 10.0 ml/min group and 28 (17%) in the TFR > 10.0 ml/min group (Table 1). Not surprisingly, patients with a TFR $\geq$10.0 ml/min were significantly more likely to have received a blood transfusion (p = 0.027). The overall difference in the rate of complications between the two groups was 2.1%. There were similar findings using CR (results not shown).

3.2. Postoperative complications

Table 2 provides the results of the logistic regression model of the effect of TFR on development of any complication, controlling for other covariates. Patients with a TFR $\geq$10.0 ml/min were significantly less likely to have a post-operative complication compared to patients with a TFR <10.0 ml/min (OR 0.24, p = 0.010). Patients with positive margins had five times higher odds of a complication compared to patients with negative margins (OR 4.91,