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Surgical Feeding Tubes in Pediatric and Adolescent Cancer Patients – A Single-Institution Retrospective Review

Emma C. Hamilton, MD^{a,*}, Thomas Curtin, BA^{b,*}, Rebecca S. Slack, MS^c, Christine Ge^b, Austen Slade, BS^a, Andrea Hayes-Jordan, MD^{a,b}, Kevin P. Lally, MD, MS^{a,b}, and Mary T. Austin, MD, MPH^{a,b}

^aDepartment of Pediatric Surgery, McGovern Medical School at The University of Texas Health Science Center at Houston, Houston, Texas

^bDepartment of Surgical Oncology, The University of Texas M.D. Anderson Cancer Center, Houston, Texas

^cDepartment of Biostatistics, The University of Texas M.D. Anderson Cancer Center, Houston, Texas

Abstract

The purpose of our study was to evaluate surgical enteric access in pediatric cancer patients to determine factors associated with postoperative complications. We performed a single institution retrospective review of all patients <21 years old with a primary cancer diagnosis who underwent surgical procedures for enteral access between 2004–2014. Multivariate logistic regression was performed to determine independent predictors of postoperative complications. During the study period, 122 patients had surgically placed feeding tubes, of whom 58% developed one or more complication(s) and 16% experienced a major complication. No single factor was significantly associated with developing any complication or major complication. Several trends were noted including increased complications associated with jejunostomy tubes, percutaneous endoscopic gastrostomy tubes, and abdominal radiation. Surgically placed enteric access in pediatric and adolescent cancer patients is associated with an extremely high complication rate emphasizing the importance of careful evaluation of these patients prior to embarking on surgical feeding access. Future work should evaluate mechanisms to decrease complications and/or explore alternative methods to provide supplemental nutrition in children and adolescents with cancer.

Keywords

enteral feeding; gastrostomy; jejunostomy; pediatric oncology

Corresponding Author: Mary T. Austin, MD, MPH, The University of Texas M.D. Anderson Cancer Center, 1400 Pressler, Unit 1406, Houston, TX 77030-1439, Telephone 713.794.4408, Fax 713.794.5720, MAustin@mdanderson.org.

*Co-first authors

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Introduction

Malnutrition, defined as undernutrition, overnutrition, or poor growth, is a major problem facing children with cancer. Methodology for nutritional assessment is heterogeneous without a standard among institutions.^{1,2} Anthropometric measurements for estimation of nutritional status include weight, height, mid-upper-arm circumference, and triceps skin fold thickness.³ At present, the World Health Organization uses Z-score cut-off values for weight-for-age, height-for-age, and weight-for-height of less than -2 SD and -3 SD to define moderate and severe malnutrition, respectively.⁴ Overnutrition or obesity is often defined as a body mass index of greater than $+2$ SD.¹ Laboratory indices such as the change in visceral proteins over time, blood glucose levels, lipid profiles, hemoglobin, and lymphocyte count are useful adjuncts for assessing nutritional status.³

Patients with malnutrition are at a higher risk of chemotherapy intolerance, infection, and tumor relapse.^{1,5–8} The prevalence of undernutrition ranges from 0% to 73% in children with malignancies while the prevalence of overnutrition is 28–78% at the end of treatment among children with malignancies.^{1,9} Malnutrition can develop as a sequela of the tumor itself or arise from various side effects of treatment such as nausea, vomiting, and mucositis.^{5,6} Patients with neurologic impairment from central nervous system tumors can also develop dysphagia and require enteral feeding access to prevent undernutrition.¹⁰ Because of the harmful effects of undernourishment among pediatric cancer patients, including increased mortality and higher risk of recurrence, additional nutritional support is often needed.^{5,6,11}

One way to improve nutritional support among pediatric oncology patients is by enteral tube feeding when oral intake is inadequate or unsafe. The different devices employed for enteral feeding are gastrostomy tube, percutaneous gastrostomy tube (PEG), jejunostomy tube, gastro-jejunal feeding tube, and Dobhoff or nasogastric tube, which all vary in the location of placement and operative technique used. When the gastrointestinal tract is able to absorb enough nutrients to meet energy requirements, enteral nutrition is the preferred solution for undernutrition.^{9,12} However, parenteral nutrition may be required in the setting of gastrointestinal failure with inadequate intestinal nutrient absorption, severe mucositis, enteritis, obstruction, typhlitis, intractable vomiting, or severe pancreatitis.¹³

While enteral feeding is presumably the most efficient method of nutritional support, surgically placed enteral feeding tubes are well known to have a high rate of complications associated with the feeding tube.^{14,15} Infections and toxicity from enteral feeding are also of concern.^{11,16} Although major postoperative complications are uncommon, the combined rate of major and minor complications has been shown to exceed 70%.^{16,17}

The risk factors related to specific complications have not been well investigated. It is important to consider the factors contributing to complications with surgical enteral feeding tube placement in order to achieve the optimal outcome for these patients. The objective of this study is to investigate and identify potential risk factors among pediatric cancer patients for post-operative complications related to surgical enteral feeding tubes.

Materials and Methods

We performed a single institutional retrospective cohort study of all patients <21 years with a primary cancer diagnosis undergoing placement of a surgical enteral feeding tube at The University of Texas MD Anderson Cancer Center (MDACC) between January 2004 and January 2014. Patients were excluded if they did not undergo placement of a gastrostomy or jejunostomy tube, if the patient underwent tube exchange only, or if access to the patient's medical record was limited. All patient records were followed from the date of tube placement for a minimum of 30 days and until the patient had the tube removed, died, or was lost to follow-up. Patients were excluded if follow-up was less than 30 days.

Demographic and clinical information were extracted from each patient record in the electronic medical record system and included age, sex, race/ethnicity, insurance type, body mass index (BMI), cancer type, and comorbidities. Similar to prior studies evaluating enteral nutrition in pediatric cancer patients, cancer type was categorized as leukemia, primary central nervous system (CNS) tumors, and non-CNS solid tumors.^{11,14,18} Patient records were also reviewed for the type of surgical technique performed. Procedures were categorized as open gastrostomy tube (Stamm gastrostomy), laparoscopic gastrostomy tube, percutaneous endoscopic gastrostomy (PEG) tube, interventional radiology placed gastrostomy tube, open jejunostomy tube, laparoscopic jejunostomy tube, separate open gastrostomy and jejunostomy tubes, and open gastro-jejunal feeding tube.

The primary outcome of interest was the frequency of any complication following placement of a surgical feeding tube. The secondary outcome of interest was the frequency of major complications. We included all perioperative complications following placement of the surgical feeding tube and complications associated with the maintenance of the feeding tube. Major complications were defined as any unplanned event resulting in admission to the hospital or a complications-related surgical or interventional procedure. Minor complications were defined as documentation of peritubal wound infection or inflammation, tube dislodgement <90 days or >90 days after placement, tube blockage requiring replacement, chronic pain, tube leakage, granulation tissue, feeding intolerance, bleeding, pneumonia, urinary tract infection, fever, other non-infectious adverse events, and other systemic adverse events. Major and minor complications were identified by a two independent reviewers of the electronic medical record for each patient. Any discrepancies of major or minor complication were decided by a third independent reviewer.

Post-operative care after placement of surgical feeding tube is not protocolized at our institution and is left up to the individual provider. All pediatric caregivers receive comprehensive in-hospital education and training about their child's surgical feeding tube, daily care, and maintenance prior to discharge. Patients are followed in the surgical clinic and timing of the first exchange of the surgical feeding tube usually occurs at 90 days postoperatively.

Patient characteristics were described through summary statistics (frequency and percentage for categorical variables, median and range for quantitative variables). All complications from the patient's first operation were plotted by frequencies for total occurrences and for

major occurrences, regardless of the number of times the complication occurred in each person. Multiple chi-square tests were performed to investigate the association between patient characteristics and having any complication related to the patient's first operation. An exploratory multivariate analysis was performed using generalized estimating equation to accommodate multiple operations per arm. However, with too few second and third operations, the intra-patient correlation could not be calculated and the model would not stabilize. We then selected each patient's first operation only and performed an exploratory logistic regression for 1) any complications and 2) major complications. Based on clinical knowledge and sample size limitations for logistic regression, surgical technique, tube position, concomitant laparotomy, abdominal radiation, and perioperative steroid use were included in the multivariate model for any complications. Tube position and surgical technique were similarly examined together for major complications. Small missing groups were excluded from consideration so that the amount of excluded missing data was never higher than 10% of the sample.

This study was approved under protocol PA14-0536 by the institutional review board at MDACC.

3. Results

A total of 159 patients were admitted to MDACC and underwent insertion of a surgical feeding tube between January 2004 and January 2014. The decision to place a surgical feeding tube was made at the discretion of the patient's treatment team. A total of 37 patients were excluded leaving a total of 122 patients included for analysis (Figure 1). Patient characteristics are summarized in Table 1. The median age at the time of operation was 12.5 years (range of 0–21 years). Most patients had a diagnosis of non-CNS solid tumor (76%, n=93), whereas 17% (21) had a CNS tumor, and 7% (8) had leukemia. Of the patients with non-CNS solid tumors, 43% (53) underwent feeding tube placement at the time of cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (HIPEC). A total of 24 (20%) patients received either neoadjuvant or adjuvant abdominal radiation therapy. The majority of these patients had desmoplastic small round cell tumors of the abdomen (n=16, 67%) and received a total of 30 Gy adjuvant whole abdomen radiation therapy. Race/ethnicity was missing for 10 patients.

The type of surgical feeding tube and the type of procedure were determined by the individual surgeon. The majority of patients underwent placement of separate gastrostomy and jejunostomy tubes (30%, n=37). Eighty-four (69%) procedures were performed open, 10 (8%) laparoscopic, and 28 (23%) endoscopic. Overall, 70 patients (58%) experienced a complication, of which 20 (16%) were a major complication. The most common minor complication was tube leakage followed by peritubal wound inflammation (Figure 2). The most common major complication was peritubal wound infection requiring admission for intravenous antibiotics followed by gastrocutaneous fistula (Figure 2). Management of enteral nutritional when a complication occurred varied according to the complication type and the individual physician's preference.

The unadjusted number of complications for each patient demographic and clinical characteristic is listed in Table 2. There were no patient or surgical factors associated with having any complications or major complications that reached statistical significance on multivariate analysis (Tables 3 and 4). However, several trends were noted including increased complications among patients with jejunostomy tubes, PEG tubes, and abdominal radiation. Furthermore, there was a trend for jejunostomy tubes to be associated with major complications. Forty percent (4) of patients with jejunostomy tubes had major complications, compared to 16% (12) of patients with gastrostomy tubes, and 11% (4) with separate gastrostomy and jejunostomy tubes ($p=0.08$). Subgroup analysis was performed excluding patients who had undergone cytoreductive surgery with HIPEC. This subgroup had a similar rate of complications as the entire cohort with 39 (60%) of patients developing any complications and 12 (18%) had major complications.

Discussion

Our experience indicates that feeding tube placement in pediatric oncology patients is associated with a high frequency of complications. In our cohort of children with a cancer diagnosis undergoing feeding tube placement, 58% (71) experienced any type of complication and 16% (20) experienced a major complication. In our multivariate analysis, patient and procedure associated risk factors for any complication were not readily identified. However, there was a trend for jejunostomy tubes, PEG tubes, and abdominal radiation to be associated with the development of any complication and placement of a jejunostomy tube to be associated with major complications.

Appropriate nutritional support is important among pediatric patients with cancer. Children with the greatest risk of undernutrition are those with Wilms' tumor, neuroblastoma, pelvic rhabdomyosarcoma, Ewing's sarcoma, non-Hodgkin's lymphoma, acute nonlymphocytic leukemia, acute lymphocytic leukemia, medulloblastoma and other brain tumors.⁹ Initiation of nutritional support is associated with several benefits including improved tolerance to chemotherapy, improved survival, increased quality of life, and decreased risk of infection in children.^{1,9} However, the timing and type of nutritional intervention is inconsistent across pediatric cancer centers.²

Surgically placed enteral feeding tubes are an option to improve nutritional support when oral intake is inadequate to support growth or nutritional repletion in a child undergoing treatment for cancer.^{9,2} In addition, enteral feeds as compared to parenteral feeds, have decreased risk of infections, liver function abnormalities, and can promote maintenance of the gut mucosa among children undergoing chemotherapy.^{14,19} However, surgically placed enteral feeding tubes are associated with a high burden of perioperative complications and long term maintenance related complications. Improved education, discharge protocols, and scheduled maintenance are possible interventions to minimize or prevent maintenance related complications.²⁰⁻²² However, while comprehensive multidisciplinary discharge protocols have demonstrated reduced emergency department visits for minor gastrostomy tube complications, they have not been able to reduce the rate of complications.²¹

Our study supports previous studies demonstrating moderately high rate of complications associated with surgical enteral feeding tubes in pediatric patients.^{6,14,16,17,19} The most common complication in our study was minor leakage around the tube followed by peritubal wound complications. Within our institution, there is no standard protocol for post-operative care for patients with enteral tube feeds which may influence the rate of complications. Complications are managed based on clinical protocols and include education of the patient's caregiver to help reduce future complications. Our findings are in agreement with previous studies conducted in pediatric oncology patients where 62–90% of patients experience a complication related to their tube.^{6,14,16,19} The most common complication in these studies was peritubal wound complications in 46–73% of patients.^{6,14,16,17,19}

The evidence examining the association of modifiable risk factors, such as type of procedure, with postoperative complications is mixed. A recent systematic review and meta-analysis of gastrostomy tubes among children demonstrated no difference in major complications between open versus laparoscopic gastrostomy tubes while PEG tubes were associated with a significantly increased risk in major complications as compared to laparoscopic gastrostomy tubes.²³ Other studies have demonstrated increased risk of infection with open as compared to laparoscopic or PEG tubes.¹⁸ In our study, PEG tubes had a higher rate of any post-operative complication as compared to open gastrostomy tubes.

The rate of major complications in our patient series is somewhat higher than other studies in pediatric oncology patients. In a series of PEG tubes in pediatric oncology patients by Schmitt et al⁶, 13% of patients had a major complication whereas 6% of patients with either a PEG or open gastrostomy had a major complication in the study by Mathew et al.¹⁴ Unlike the series by Schmitt et al⁶ and Mathew et al¹⁴, our series included patients with jejunostomy tubes.^{6,14} Although it did not reach statistical significance, placement of a jejunostomy tube was the strongest predictor of any complication and of a major complication in our study. Previous studies have demonstrated rates of major complications related to jejunostomy tube placement in children of approximately 22–24%.^{24,25} The observed major complication rate of 40% among patients with jejunostomy tubes in our series is possibly due to small patient volume and differences in patient selection. Adult studies among patients undergoing placement of jejunostomy tube at the time of oncologic resection have demonstrated increased complications and length of stay.^{26–28}

To our knowledge, this is the largest series evaluating risk factors for complications after surgical enteral feeding tube placement in pediatric oncologic patients undergoing cytoreductive surgery with HIPEC. Cytoreductive surgery is the complete surgical resection of all visible disease with administration of hyperthermic intraperitoneal chemotherapy in patients with peritoneal carcinomatosis.²⁹ Information about feeding tubes in this patient population is limited, especially among pediatric patients. In a study of adult patients undergoing cytoreductive surgery and HIPEC for peritoneal carcinomatosis from a colorectal primary cancer, routine placement of a feeding tube did not demonstrate improved nutritional outcomes and was associated with increased length of stay and higher 30-day and 60-day readmission rates.²⁷ In our series, undergoing feeding tube placement with concomitant laparotomy including cytoreductive surgery with HIPEC was not associated with an increased risk of post-operative complications.

Our single-center retrospective study is subject to limitations associated with data not prospectively collected. Furthermore, there is no protocol in place for placement of a surgical enteral feeding tube in pediatric oncology patients. The decision to place a surgical enteral feeding tube and the surgical technique may vary among oncologists and surgeons. In addition, we were not able to control for operative factors that may influence the development of postoperative complications. Also, the patient data were limited to information available in the electronic medical record. Markers of pre-operative nutritional status including anthropometric measurements and laboratory data were limited in the medical record and could not be included in our multivariate analysis. In addition, complications that occurred among patients discharged home on enteral nutrition may not have been captured if the patient was evaluated at an outside facility. The average length of follow-up and the average length of nutritional support before a complication occurred were also missing for several patients.

Conclusions

Ensuring pediatric oncologic patients maintain adequate nutrition during the course of their treatment is essential. However, placement of a surgical enteral feeding tube in this population is associated with a high rate of both minor and major complications. Understanding the burden of perioperative and maintenance related complications is critical when deciding to place a surgical enteral feeding tube. Furthermore, identifying modifiable risk factors for complications is important for improving outcomes. This study suggests that jejunostomy tubes and PEG tubes may be associated with increased complications. Future studies are needed to further understand the associated risks and benefits of surgical enteral feeding tubes in pediatric oncologic patients.

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Figure 1.
Patient Flow Diagram of Inclusion and Exclusion

Figure 2.
Distributions of Minor and Major Complications

Table 1**Patient Characteristics at the Time of Procedure**

Patient Characteristics	All Patients N (%)
All	122 (100%)
Age – median (min, max)	12.5 (0, 21)
Age Group	
0–10 years	51 (42%)
11+ years	71 (58%)
Gender	
Female	63 (52%)
Male	59 (48%)
Race/Ethnicity	
White	78 (70%)
Black	12 (11%)
Hispanic	12 (11%)
Other	10 (9%)
Insurance at First Surgery	
Medicaid	21 (17%)
Private	81 (67%)
Self-pay	20 (16%)
BMI – median (min, max)	17.7 (11.9, 44.6)
Cancer	
Leukemia	8 (7%)
Solid Tumor CNS	21 (17%)
Solid Tumor Non-CNS	93 (76%)
Comorbidities *	
Asthma	5 (4%)
GERD	7 (6%)
Obesity (BMI ≥ 30)	6 (5%)
Neutropenia (ANC < 1000)	5 (4%)
Thrombocytopenia (Plt < 50,000)	7 (6%)
Type of Procedure	
GJ-Open	20 (17%)
GT-Lap	8 (7%)
GT-Open	19 (16%)
GT-Open & JEJ-Open	37 (30%)
JEJ-Lap	2 (2%)
JEJ-Open	8 (7%)
IR Gastrostomy	21 (17%)
PEG	7 (6%)
Abdominal XRT	

Patient Characteristics	All Patients N (%)
Yes	24 (20%)
Steroid Use	
Yes	20 (16%)
Systemic Chemotherapy*	
Conventional	49 (40%)
mTOR Inhibitor	56 (46%)
TKI	3 (2%)
Immune Modulator	2 (2%)
Monoclonal Antibody	1 (1%)
Proteasome Inhibitor	1 (1%)
Concomitant Surgery	
Ex-lap with tumor resection	9 (7%)
Ex-lap, other	2 (2%)
HIPEC, cytoreductive	53 (43%)
Port placement	13 (11%)
None	45 (37%)

* Patients may have none, one, or more comorbidities or chemotherapy treatments

Abbreviations: BMI= body mass index; CNS= central nervous system; GERD= gastroesophageal reflux disease; ANC= absolute neutrophil count; Plt= platelet; GJ= gastro-jejunal feeding tube; GT=gastrostomy tube; JEJ=jejunostomy tube; PEG= percutaneous endoscopic gastrostomy tube; Lap=laparoscopic; XRT= radiation; mTOR= mammalian target of rapamycin; TKI=tyrosine kinase inhibitor

Table 2

Surgery Complications by Patient Characteristics for First Surgeries Only

Patient Characteristic	Any Complications			Major Complications		
	N (%)	N (%)	P-Value	N (%)	N (%)	P-Value
All	122 (100%)	71 (58%)		20 (16%)		
Age			0.17			0.86
0–10 years	51 (42%)	26 (51%)		8 (16%)		
11+ years	71 (58%)	45 (63%)		12 (17%)		
Gender			0.54			0.07
Female	63 (52%)	35 (56%)		14 (22%)		
Male	59 (48%)	36 (61%)		6 (10%)		
Race/Ethnicity			0.21			0.97
White	78 (70%)	49 (63%)		13 (17%)		
Black	12 (11%)	6 (50%)		2 (17%)		
Hispanic	12 (11%)	4 (33%)		2 (17%)		
Other	10 (9%)	7 (70%)		1 (10%)		
Insurance			0.80			0.42
Medicaid	21 (17%)	12 (57%)		2 (10%)		
Private	81 (66%)	46 (57%)		13 (16%)		
Self-pay	20 (16%)	13 (65%)		5 (25%)		
Cancer			0.32			0.69
Leukemia	8 (7%)	3 (38%)		1 (13%)		
Solid Tumor CNS	21 (17%)	11 (52%)		2 (10%)		
Solid Tumor Non-CNS	93 (76%)	57 (61%)		17 (18%)		
Asthma			0.65			0.59
Yes	5 (4%)	2 (40%)		0 (0%)		
No	117 (96%)	69 (59%)		20 (17%)		
GERD			>0.99			0.60
Yes	7 (6%)	4 (57%)		2 (29%)		
No	115 (94%)	67 (58%)		18 (16%)		

Patient Characteristic	Any Complications		Major Complications	
	N (%)	P-Value	N (%)	P-Value
Overweight/Obese		0.58		0.71
Yes	15 (12%)	10 (67%)	3 (20%)	
No	107 (88%)	61 (57%)	17 (16%)	
Neutropenia		0.65		>0.99
Yes	5 (4%)	2 (40%)	1 (20%)	
No	116 (96%)	68 (59%)	18 (16%)	
Thrombocytopenia		0.70		0.59
Yes	7 (6%)	5 (71%)	2 (29%)	
No	114 (94%)	65 (57%)	17 (15%)	
Surgical Technique		0.48		0.79
Endoscopic	28 (23%)	19 (68%)	4 (14%)	
Laparoscopic	10 (8%)	5 (50%)	1 (10%)	
Open	84 (69%)	47 (56%)	15 (18%)	
Tube Location		0.24		0.08
Jejunostomy	10 (8%)	8 (80%)	4 (40%)	
Gastrostomy	75 (61%)	40 (53%)	12 (16%)	
Separate Gastrostomy and Jejunostomy	37 (30%)	23 (62%)	4 (11%)	
Type of Physician		0.47		0.75
Radiologist	21 (17%)	14 (67%)	4 (19%)	
Surgeon	101 (83%)	57 (56%)	16 (16%)	
Abdominal XRT		0.18		0.54
Yes	24 (20%)	17 (71%)	5 (21%)	
No	98 (80%)	54 (55%)	15 (15%)	
Steroid Use *		0.81		>0.99
Yes	20 (16%)	11 (55%)	3 (15%)	
No	102 (84%)	60 (59%)	17 (17%)	
Conventional Chemotherapy *		0.58		>0.99
Yes	49 (40%)	27 (55%)	8 (16%)	
No	73 (60%)	44 (60%)	12 (16%)	

Patient Characteristic	Any Complications			Major Complications		
	N (%)	N (%)	P-Value	N (%)	P-Value	
mTOR Inhibitor *			0.71			0.81
Yes	56 (46%)	34 (61%)		10 (18%)		
No	66 (54%)	37 (56%)		10 (15%)		
TKI *			>0.99			>0.99
Yes	3 (2%)	2 (67%)		0 (0%)		
No	119 (98%)	69 (58%)		20 (17%)		
Immune Modulator *			0.51			>0.99
Yes	2 (2%)	2 (100%)		0 (0%)		
No	120 (98%)	69 (58%)		20 (17%)		
Proteasome Inhibitor			>0.99			>0.99
Yes	1 (1%)	1 (100%)		0 (0%)		
No	121 (99%)	70 (58%)		20 (17%)		
Monoclonal Antibody *		0.42		>0.99		
Yes	1 (1%)	0 (0%)		0 (0%)		
No	121 (99%)	71 (59%)		20 (17%)		
Concomitant Surgery			>0.99			0.81
Large Ex-lap	64 (52%)	37 (58%)		11 (17%)		
No Concomitant Abdominal	58 (48%)	34 (59%)		9 (16%)		

* Use of these medications is perioperative and is "Yes" if they appear in the patient records 0 days, 7 days or 30 days prior to surgery

Abbreviations: CNS= central nervous system; GERD= gastroesophageal reflux disease; XRT= radiation; mTOR= mammalian target of rapamycin; TKI=tyrosine kinase inhibitor; Ex-lap= exploratory laparotomy

Table 3

Multivariate Prediction of Any Surgery Complication by Patient Characteristics

Patient Characteristics		Odds ratio (95% CI)	P-value
Concomitant Laparotomy	Yes vs No	0.94 (0.32, 2.77)	0.91
Steroid Use	Yes vs No	1.15 (0.41, 3.27)	0.79
Tube Position	Both vs Stomach	1.99 (0.70, 5.68)	0.80
	Jejunum vs Stomach	5.31 (0.93, 30.30)	0.12
Surgical Technique	Endo vs Open	3.01 (0.97, 9.35)	0.06
	Lap vs Open	1.08 (0.24, 4.83)	0.51
Abdominal XRT	Yes vs No	2.36 (0.82, 6.80)	0.11

Abbreviations: Endo=endoscopic; Lap=laparoscopic; XRT= radiation

Table 4

Multivariate Prediction of Major Surgery Complication by Patient Characteristics

Patient Characteristic		Odds ratio (95% CI)	P Value
Tube Position	Both vs Stomach	0.52 (0.14, 1.90)	0.06
	Jejunum vs Stomach	3.44 (0.76, 15.52)	0.04
Surgical Technique	Endo vs Open	0.71 (0.19, 2.65)	0.80
	Lap vs Open	0.33 (0.04, 3.06)	0.41

Abbreviations: Endo=endoscopic; Lap=laparoscopic;