# Ellen M. Cosgrove Research Competition

## Manuscript Competition

| **Title of Submission** | Gastrointestinal Bleeding following Colorectal Surgery with Stapled Anastomosis | | | |
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| **Role** *Author, Mentor, Faculty, Other* | **Full First Name** | **Full Last Name** | **Degree** | **Institution** |
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**Deadline for Submission is Thursday, May 4, 2017 NOON**
**Award Ceremony Monday, June 5, 2017**

**Title:** Gastrointestinal Bleeding following Colorectal Surgery with Stapled Anastomosis

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**Introduction:** Gastrointestinal bleeding (GIB) following colorectal surgery can increase length of hospital stay, lead to interruption of thromboembolism prophylaxis, and subject patients to risks associated with blood transfusion. This study aims to identify the incidence of, and risk factors for GIB following elective colorectal surgery with primary anastomosis.
**Methods**: Elective colorectal resections with ileocolic or colorectal anastomoses performed by two fellowship-trained colorectal surgeons from 3/2013-5/2016 were included. Electronic medical records were reviewed to determine whether GIB occurred post-operatively. Multiple variables were analyzed (Table 1) including patient-, operative-, and post-operative factors. Secondary endpoints include the need for blood transfusion and average length of hospital stay. Confidence intervals with $\alpha = 0.05$ were compared to determine statistical significance.
**Results:** 244 patients underwent elective colorectal resection with either ileocolic or colorectal anastomosis. Sixty-six ileocolic and 178 colorectal anastomoses were performed using linear or circular stapling devices, respectively. Overall, 19.3% of patients reported GI bleed ranging from post-operative day zero to eleven. Only 1,6% required blood transfusion. Length of hospital stay did not vary significantly between the GIB and Non-GIB groups. None of the patient-, operative-, or post-operative factors examined were found to correlate significantly with post-operative GIB.
**Conclusion:** Post-operative GIB after colorectal surgery did not significantly increase length of hospital stay or need for blood transfusion as compared to those patients without GIB. Further study is needed to elucidate risk factors associated with GIB after stapled anastomosis.

## Introduction:

Gastrointestinal bleeding (GIB) is one of the most common complications following colorectal surgery with a reported incidence up to 5.5%[1]. Clinically significant GIB can presumably increase length of hospital stay, lead to interruption of venous thromboembolism (VTE) prophylaxis, and subject patients to risks associated with blood transfusion. Risk factors associated with post-operative anastomotic hemorrhage have not been well defined in the literature nor has the relationship to length of hospital stay. This study aims to identify the incidence of, and risk factors for GIB following elective colorectal surgery with primary anastomosis. The need for blood transfusion and other therapeutic interventions is also recorded.

## Methods:

This retrospective study examines elective colorectal resections performed by two fellowship-trained colorectal surgeons between March 2013 and May 2016. Inclusion criteria included patients greater than 18 years of age with a single ileocolic or colorectal anastomosis. Electronic medical records were reviewed to divide patients into two groups based on whether or not they experienced GIB post-

operatively, defined as any gross bleeding per rectum recorded in daily progress notes. Multiple variables were analyzed (Table 1) including patient-, operative-, and post-operative factors.

Patient factors include demographic data such as age, sex, American Society for Anesthesiologists (ASA) physical assessment classification, body mass index (BMI), presence of diabetes, smoking status, and pathology (benign vs. malignant). Pre-operative use of anti-coagulation or platelet-inhibiting medication were also compared between groups. Patients were routinely asked to hold anti-platelet therapy and anti-coagulation pre-operatively.

Operative factors include anastomotic site, operative time, and estimated blood loss (EBL). Ileocolic anastomoses were performed using linear staplers in a side-to-side, functional end-to-end fashion while colorectal anastomoses were created using circular staplers in and end-to-end fashion.

Post-operative factors include the use of venous thromboembolism (VTE) prophylaxis or other anticoagulation or platelet-inhibiting medications. VTE prophylaxis with subcutaneous heparin or low-molecular weight heparin (LMWH) was routinely initiated within twelve hours of operation. The timing of post-operative initiation of anticoagulation or platelet-inhibiting medication was recorded.

Secondary endpoints include the need for post-operative blood transfusion and average length of hospital stay. Among the GIB group, we also examine how often post-operative GIB results in suspension of VTE prophylaxis and need for further intervention. Confidence intervals (CI) with $\alpha = 0.05$ were compared to determine statistical significance. Institutional review board exemption was formally granted.

**Results:**

Two hundred and forty-four patients underwent elective colorectal resection with either ileocolic or colorectal anastomosis during the study period. Sixty-six ileocolic and 178 colorectal anastomoses were performed using linear or circular stapling devices, respectively. Overall, forty-seven patients (19.3%) reported GIB ranging from post-operative day zero to eleven with average date of bleed occurring on the second post-operative day. Of these, only four (1.6% of total) were significant enough to required blood transfusion and one patient required endoscopic treatment.

There was no significant difference between GIB and non-GIB groups in terms of patient age, sex, ASA classification, BMI, smoking status, or percentage of patients with diabetes or malignant surgical indication (Table 1). Similar proportion of patients in each group had been on anti-coagulation or platelet-inhibiting medication pre-operatively (Table 1). No patients in the GIB group were noted to have bleeding diatheses.

The GIB and non-GIB groups were comprised of similar rates of ileocolic and colorectal anastomoses (Table 1). Patients with colorectal anastomoses were no more likely to experience GIB than those with ileocolic anastomoses; GIB was noted in 9 of 66 patients with ileocolic anastomosis (13.6%; 95% CI [1.1%, 26.1%]) and 38 of the 178 patients with colorectal anastomosis (21.3%; 95% CI [8.3%, 34.4%]). Intra-operative factors including estimated blood loss and operative time were also similar between groups (Table 1). Laparoscopy or robotic

assistance was utilized in 93.6% of GIB group (95% CI [85.5, 100]) and did not differ significantly from the non-GIB group (94.9%; 95% CI [91.3, 98.5]).

Pharmacological VTE prophylaxis was initiated in all patients in the GIB group and 99% of the patients without GIB (remaining patients refused DVT prophylaxis). Within the GIB group, VTE prophylaxis was withheld in 32 patients (68.1%; 95% CI [53.3%, 82.9%]), a significantly higher proportion than in the non-GIB group in which VTE prophylaxis was interrupted in 18 patients (9.1%; 95% CI [4.5, 13.9]). For those patients in whom platelet-inhibiting medication was initiated, the post-operative day of initiation did not vary significantly between GIB and non-GIB groups (Table 1). Therapeutic anticoagulation with warfarin or other agents was not initiated in any patients in the GIB group during their hospital stay. Therapeutic anticoagulation was initiated on post-operative day two on average when started in non-GIB group patients.

Blood transfusion was required in four patients in GIB group (8.5%; 95% CI [0,17.4]) and in fifteen patients in the non-GIB group for dropping hematocrit post-operatively (7.6%; 95% CI [3.2, 12.0]). Length of hospital stay did not vary significantly between the GIB (3.9 days; 95% CI [0, 9.6]) and Non-GIB (4.6 days; 95% CI [0, 21.7]) groups. There were no mortalities among the GIB group. Bleeding stopped spontaneously in all GIB patients with the exception of one who required endoscopic intervention. No patients in GIB group experienced VTE or PE in post-operative period.

**Discussion:**

GIB from anastomotic staple line following colorectal surgery is a common post-operative phenomenon ranging from minor hematochezia with first bowel movement to significant hemorrhage requiring transfusion of blood products and occasionally further intervention in the form of endoscopic therapies, angiographic embolization, or surgical refashioning of anastomosis.

The rate of major gastrointestinal hemorrhage following colorectal anastomosis ranges from 0.5-5.5%[1-5]. The rate of minor bleeding following colorectal surgery with stapled anastomosis has not been well defined in the literature but was found to be as high as 17.6% of patients in this study. Major hemorrhage, defined as those requiring transfusion for post-operative GIB occurred in only 1.6% of patients. By some estimation, approximately 50% of patients with minor bleeding eventually progress to major bleeding requiring blood transfusion[3]. This was not borne out by the present study.

Anastomotic bleeding may be due in part to inadequate clearance of mesentery prior to bowel division, and there is some evidence that GIB is less common following stapled anastomosis[4]. However, a Cochrane review evaluating only ileocolic anastomoses found that there was no difference in the rate of anastomotic hemorrhage when comparing stapled to hand-sewn anastomoses; of 65 patients included in their analysis, however, no hemorrhage was recorded in either group[6]. In a Cochrane review of stapled versus hand-sewn techniques for colorectal anastomoses, anastomotic hemorrhage was found in 5.4% (18 of 336 patients) versus 3.1% (10 of 326), respectively, which did not reach statistical significance[2].

In their analysis of 350 patients undergoing right hemicolectomy, Golda et. al. found that end-to-side, circular, double-stapling technique for ileocolic anastomosis was associated with increased

incidence of anastomotic hemorrhage (4.9%) as compared to linear side-to-side or handsewn techniques (0%, 0%, respectively)[7]. In the present study, all ileocolic anastomoses were created using linear staplers in a side-to-side fashion while all colorectal anastomoses were created using an end-to-end stapling device. There was no significant difference in the rate of GIB between the two techniques. Three of the four patients with GIB requiring transfusion had colorectal anastomoses.

Risk factors associated with anastomotic GIB have not been well defined in the literature. Golda et. al. also identified COPD as a predictive factors for postoperative lower GIB. They also found a trend toward more GIB in patients receiving preoperative vitamin K antagonist anticoagulation; GIB occurred in 11.5% (3 of 26) as compared with 4.3% (14 of 324) of those not taking anticoagulant therapy. However, these differences were not statistically significant[7]. Similarly, the present study did not see a difference in GIB rate among patients on pre-operative anticoagulation or anti-platelet therapy, which were routinely held preoperatively.

Blood transfusion following rectal resection for cancer has been reported as high as 20-75%[8]. In addition to risks of transfusion reaction and infection transmission, some authors have found that allogenic red blood cell transfusions adversely affects host immune function and is an independent predictor of earlier recurrence or cancer related death[9-13]. In a multivariate analysis of 212 patients undergoing resection for rectal cancer, Benoist et. al identified five independent risk factors for peri-operative blood transfusion: age >65 years, BMI >27 kg/m$^2$; pre-operative hemoglobin less than 12.5 g/dL, ASA status >2, and additional surgical procedures[8]. None of the risk factors evaluated in the present study were significantly associated with GIB. Average pre-operative hemoglobin for patients requiring transfusion was 13.6 g/dL. Interestingly, patients with anastomotic hemorrhage did not receive post-operative transfusion at a higher rate than their counterparts as the majority of these patients experienced minor GIB only.

Most GIB following colorectal surgery will stop spontaneously with conservative measures[4]. Early post-operative endoscopy has been found to be safe as a means of localizing the hemorrhage, assessing the risk of re-bleeding, and utilizing endoscopic measures to gain hemostasis[8,14]. The safety of post-operative colonoscopy has also been demonstrated in animal model after left colectomy[15]. Other modalities described to obtain hemostasis include infusion of epinephrine solution through rectal tube[16].

A prospective collection of 777 patients over 15 years found that only 6 patients (0.8%) developed anastomotic hemorrhage within twenty-four hours of surgery that required intervention other than transfusion. Three of these patients were treated with endoscopic diathermy coagulation or clipping while the other three patients required anastomotic revision[4]. It has been reported that suture dehiscence rate was more than 3-fold higher in the presence of lower GIB[7]. While endoscopic electrocoagulation has been deemed safe and effective in controlling unremitting hemorrhage in the early post-operative period, there have also been reports of anastomotic leaks and anastomotic fistula development after endoscopic treatment of post-operative GIB[3,17].

Colorectal surgery has been at the forefront of "enhanced recovery pathways," standardized protocols for pre-operative, intra-operative, and post-operative care as a means to shorten hospital length of stay and reduce readmission[18]. In a SEER-Medicare database analysis 149,622

patients with colonic adenocarcinoma who underwent surgical resection with curative intent from 1986-2005, it was noted that mean LOS decreased a significant amount over time from 14.0 days in 1986-1990 to 10.6 days from 2001-2005[1]. GIB was not associated with increased LOS in the present study with overall mean LOS of 4.4 days.

One-third of the nearly 200,000 VTE-related deaths per year in the United States occur following surgery[19]. Up to 40% of patients undergoing general surgical procedures will develop a DVT without prophylaxis, and this risk doubles in the presence of malignant disease. The American College of Chest Physicians recommends pharmacologic DVT prophylaxis for all patients undergoing general surgery who are at moderate or high risk for DVT[20].

In a systematic review of 33 randomized controlled trials (RCTs) studying VTE prophylaxis, it was noted that bleeding complications occur less than 3% of patients undergoing general surgical procedures. GIB occurred in 0.2% of 12,928 patients in 6 of these RCTs. Pharmacological VTE prophylaxis was discontinued in 2.0% of 10,540 patients[21]. In the present study, VTE prophylaxis was held in 68.1% of patients with GIB. None of these patients went on to develop VTE.

**Conclusion:**
Post-operative GIB after colorectal surgery did not significantly increase length of hospital stay or need for blood transfusion as compared to those patients without GIB. Further study is needed to elucidate risk factors associated with GIB after stapled anastomosis.

Table 1. Patient-, Operative-, and Post-operative Risk Factors

| | GIB (95% CI) | Non-GIB (95% CI) | p-value |
|---|---|---|---|
| **Age (years)** | 58.7 (34.1, 83.3) | 62.2 (34.7, 89.7) | >.05 |
| **Sex (% female)** | 55.3% (39.5, 71.1) | 54.3% (46.1, 62.6) | >.05 |
| **ASA** | 2.2 (1.4, 3.0) | 2.3 (1.3, 3.2) | >.05 |
| **BMI** | 27.2 (16.8, 37.7) | 28.7 (15.5, 41.9) | >.05 |
| **Diabetes** | 14.9% (3.6, 26.2) | 18.3% (11.9, 22.4%) | >.05 |
| **Smokers** | 12.8% (2.2, 23.4) | 16.2% (10.1, 22.4) | >.05 |
| **Malignant** | 19.1% (6.6, 31.7) | 38.6% (30.5, 46.6) | >.05 |
| **Anti-Platelet Pre-op** | 14.9% (3.6, 26.3) | 12.2% (6.8, 17.6) | >.05 |
| **Anticoagulation Pre-op** | 2.1% (0.0, 6.7) | 3.6% (0.5, 6.6) | >.05 |
| **OR Time (min)** | 233 (128, 338) | 237 (114, 360) | >.05 |
| **EBL (cc)** | 83 (0, 252) | 113 (0, 418) | >.05 |
| **Ileocolic anastomosis** | 20.9% (7.3, 34.6) | 28.4% (21.0, 35.7) | >.05 |
| **Colorectal anastomosis** | 79.1% (13.7, 65.4) | 71.6% (7.4, 64.3) | >.05 |
| **VTE Prophylaxis** | 100% (100, 100) | 99% (97.3, 100) | >.05 |
| **Anti-PLT Post-op Day** | 4 (0.6, 7.4) | 3.1 (0.0, 6.3) | >.05 |
| **Anticoag Post-op Day** | N/A | 2.4 (0.0, 4.9) | >.05 |

Table 2. Results

| | GIB (95% CI) | Non-GIB (95% CI) | p-value |
|---|---|---|---|
| **LOS (day)** | 3.9 (0, 9.6) | 4.6 (0, 21.6) | >.05 |
| **Transfusion** | 8.5% (0, 17.4) | 7.6% (3.2, 12.0) | >.05 |
| **VTE prophylaxis interruption** | 68.1% (53.3, 82.9) | 9.1% (4.8, 13.9) | <.05 |

**References:**


1. Schneider E, Hyder O, Brooke B, Efrom J, Cameron J, Edil B, Schulick R, Choti M, Wolfgang C, Pawlik T. "Patient Readmission and Mortality and Colorectal Surgery for Colon Cancer: Impact of length of Stay Relative to Other Clinical Factors". *J Am Coll Surg*. 2012. 214;390-399.
2. Neutzling CB, Lusosa SAS, Proenca IM, da Silva EMK, Matos d. "Stapled versus handsewn methods for colorectal anastomosis surgery" □*Cochrane Database Syst Rev* 2012; Issue 2. Art. No.: CD003144. DOI: 10.1002/14651858.CD003144.pub2
3. Cirocco WC, Golub RW. "Endoscopic treatment of post-operative hemorrhage from a stapled colorectal anastomosis. *Am Surg*. 1995. 61:460-463
4. Malik AH, East JE, Buchanan GN, Kennedy RH. "Endoscopic haemostasis of staple-line haemorrhage following colorectal resection". *Colorectal Dis*. 2008. 10(6):616.

5. Martinez-Serrano MA, Pares D, Pera M, Pascual M, Courtier R, Gil Egea MJ, Grande L. "Management of lower gastrointestinal bleeding after colorectal resection and stapled anastomosis". *Tech Coloproctol.* 2009. 13:49-53.
6. Choy PY, Bissett IP, Docherty JG, Parry BR, Merrie AE. "Stapled versus handsewn methods for ileocolic anastomoses". Cochrane Database Syst Rev. 2007.
7. Golda T, Zerba C, Kreisler E, Trenti L, Biondo S. "Incidence and management of anastomotic bleeding after ileocolic anastomosis". *Colorectal Disease.* 2013. 15:1301-1308.
8. Benoist S, Panis Y, Panneeon V, Alves A, Valleur P. "Predictive factors for perioperative blood transfusion in rectal resection for cancer: a multivariate analysis of a group of 212 patients". *Surgery.* 2001. 129:433-439.
9. Cata J, Wang H, Gottumkala V, Reuben J, Sessler D. "Inflammatory response, immunosuppression, and cancer recurrence after perioperative blood transfusions. *Br J Anaesth.* 2013. 110(5):690-701.
10. Busch OR, Hop WC, Marquet RL, Jeekel J. "Blood transfusions and local tumor recurrence in colorectal cancer. Evidence of a non- causal relationship". *Ann Surg* 1994; 220: 791–7 .□
11. Amato A, Pescatori M. "Perioperative blood transfusions for the recurrence of colorectal cancer". Cochrane Database Syst Rev. 2006; Jan: CD005033.□
12. Edna TH, Bjerkeset T. "Perioperative blood transfusions reduce long-term survival following surgery for colorectal cancer". *Dis Colon Rectum* 1998;41:451-9.□
13. Acheson AG, Brookes MJ, Spahn DR. "Effects of allogeneic red blood cell transfusions on clinical outcomes in patients undergoing colorectal cancer surgery: a systematic review and meta-analysis". *Ann Surg.* 2012. 256(2): 235-244.
14. Mayer G, Lingenfelser T, Ell C. "The role of endoscopy in early postoperative haemorrhage". *Best Pract Res Clin Gastroenterol.* 2004. 18(5)799-807.
15. Chardavoyne R, Stein TA, Ratner LE, Bank S, Wise L. "Is colonoscopy safe in the early postcolectomy period?" *Am Surg* 1991; 57: 734–6.
16. Dietz, DW, Bailey, HR. "Postoperative complications". In: ASCRS Textbook of Colon and Rectal Surgery, Church, JM, Beck, DE, Wolff, BG, Fleshman, JW, Pemberton, JH, (Eds), Springer-Verlag New York, LLC, New York 2006. p.141.
17. Aurello P, D'Angelo R, Pozzi G et al. Terapia dell'emorragia anastomotica massiva dopo resezione retto-colica anteriore meccanica. *G Chir* 1991. 12:164-165
18. Spanjersberg WR, Reurings J, Keus F, van Laarhoven CJHM. "Fast track surgery versus conventional recovery strategies for colorectal sur□gery". Cochrane Database Syst Rev 2011 Feb 16;(2):CD007635.
19. Gould M, Garcia D, Wren S, Karanicolas P, Arcelus J, Heit J, Samana C. "Prevention of VTE in Nonorthopedic surgical patients; Antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians Evidence-based clinical practice guidelines". *Chest.* 2012;141(2_suppl):e227S-e277S.
20. Geerts WH, Pineo GF, Heit JA, Bergqvist D, Lassen MR, Colwell CW, Ray JG. "Prevention of venous thromboembolism: the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy". *Chest.* 2004;126(suppl):338S-400S.
21. Leonardi M, McGory M, Ko C. "The rate of bleeding complications after pharmacologiv deep venous thrombosis prophylaxis; a systemic review of 33 randomized controlled trials". *Arch Surg.* 2006. 141:790-799.