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Original Research Article

Early detection of anastomotic leakage after hand-sewn colorectal anastomoses

Ayman A. Albatanony[1], Mahmoud A. Shahin[1], Mohamed M. Balpoush[2]*

Department of General Surgery, [1]Faculty of Medicine, Menoufia University, Menoufia, [2]Mansoura International Hospital, Mansoura, Dakahleia, Egypt

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***Correspondence:**
Dr. Mohamed M. Balpoush,
E-mail: m.balboush@gmail.com

ABSTRACT

Background: Colorectal anastomotic leakage is a serious complication leading to major postoperative morbidity and mortality. In the present study, author investigated the early detection of anastomotic leakage before its clinical presentation.
Methods: This prospective study was including 80 consecutive patients with colorectal anastomoses using hand sewn technique. Patients follow-up was done to detect postoperative leak, study variables included hospital stay, wound infection, postoperative daily C-reactive protein, parameters of DULK-score and microbiological study of peritoneal fluid.
Results: Clinically evident AL occurred in twelve patients (15%) and diagnosed postoperatively on median day 6. The median interval between appearance of the initial signs of clinical deterioration and the confirmation of AL was three days using DULK-score. C-reactive protein was significantly higher in patients with leakage with a cut-off value of 120 mg/l on 3rd postoperative day. Intraperitoneal bacterial colonization was significantly higher in patients with clinical evidence of AL (p value 0.012). Wound infection was significantly higher in anastomotic leakage group (p value 0.001). The hospital stay for the patients with anastomotic leakage was significantly longer than those without AL (p value 0.001).
Conclusions: Routine application of DULK-score leads to diagnosis of AL three days earlier. C-reactive protein is a simple way to ensure a safe discharge from hospital after colorectal surgery.

Keywords: Anastomotic leakage, Bacterial colonization, Colon leakage score, C-reactive protein, DULK scores

INTRODUCTION

Anastomotic leakage after large bowel resection remains one of the most serious complications despite recent advances in colorectal surgery. The frequency of its incidence ranges from 2% to 24% with higher rate for rectal anastomosis than for colonic anastomosis.[1] Anastomotic leaks place a heavy burden on the patient and surgeon. Major disruptions typically present early and necessitate prompt and aggressive intervention to prevent the development of sepsis and multiorgan failure. Conservative treatment is associated with higher mortality except in minor leaks, which present rather late in the post-operative period and typically require deliberate, thoughtful and individualized management decisions.[2]

The colon leakage score (CLS) can predict the risk of anastomotic leakage following left sided colorectal surgery. After further validation, this score may help the surgeon make a more individualized, safer decision regarding whether to perform an anastomosis or a make a (de-functioning) stoma.[3]

A standardized postoperative score, the DULK (Dutch leakage) score, has been demonstrated to be a useful clinical tool in the diagnosis of anastomotic leakage.[4]

E. coli and *E. faecalis* can be detected in drainage fluid after colorectal surgery by means of culture. Therefore, these bacteria are well suited to serve as indicator organisms for diagnosis of anastomotic leakage on peritoneal drainage fluid.[5]

Early and persistent elevation of C-reactive protein after colorectal surgery with anastomosis has been used as a marker of anastomotic leakage.[6]

Author aimed in this study to evaluate the factors used for early diagnosis of anastomotic leakage after Hand-Sewn colorectal anastomoses.

METHODS

This prospective study was including 80 consecutive patients with colorectal anastomoses using hand sewn technique. Patients were operated at Menoufia University Hospital, Shibin Alkom and Mansoura International Hospital, Mansoura, Egypt from April 2016 to October 2018.

All operations were carried out by a consultant of gastrointestinal surgery who guaranteed adequate exposure and access, gentle handling of the bowel, adequate hemostasis, approximation of well-vascularized bowel, absence of tension at anastomosis, good surgical technique and avoidance of fecal contamination.

Intraoperative testing of anastomosis was done. In addition to the demographic data, other risk factors were collected, such as age, sex, body mass index (BMI), toxic habits (alcohol and tobacco), The American Society of Anesthesia (ASA) scale, need for perioperative transfusion, neoadjuvant therapy, indication for surgery, surgical procedure performed, intention of the surgery, surgical technique, type of anastomosis, complications during surgery, operating time, use of drain tubes, distance to anal margin and tumor stage.

Informed consent was obtained from all patients to be included in the study, after explanation of the nature of the disease and possible treatment.

Patients underwent colorectal surgery including emergency and elective surgeries, and both sexes and all ages were included.

Hemodynamically unstable patients e.g., patients with septic shock, sever polytraumatized patient with multiple abdominal organ affection were excluded.

All patients were subjected to preoperative assessment in the form of history taking, general and local clinical examination and investigations in the form of laboratory and radiological (distal loopogram, metastatic workup), operation where all patients were operated after performing the definitive therapeutic surgery which requires resection, hand sewn intestinal anastomosis using Vicryl 2/0 was done in double layer interrupted anastomosis.

Intraoperative leak test to confirm adequacy of anastomosis and post-operative follow up in which all patients were evaluated daily at the first 5 days postoperative regarding fever, heart rate, blood pressure, respiratory rate, urine output, mental status, nutritional status, signs of ileus (abdominal distention, vomiting, constipation), abdominal pain, signs of infection (increased leukocytic count), kidney function (increased urea and creatinine), frank anastomotic leak, surgical site infection, wound dehiscence and burst abdomen. Daily c-RP postoperative for 5 days.

Microbiological study of peritoneal fluid (aerobic and anaerobic cultures were done from the drain fluid on days 1, 3 and 5 postoperative).

In statistical analysis, data was collected prospectively. Statistical analysis of tables was performed using statistical Package for Social Sciences (SPSS for Windows, v.19.0; Chicago, IL, USA). Statistically described in terms of range, mean, standard deviation (SD), median, frequencies (number of cases) and percentages when appropriate. Comparison of quantitative variables between the study groups was done using the student t-test. P-value less that 0.05 was considered statistically significant.

RESULTS

Present study included 80 patients, who underwent large intestinal anastomosis during the period from April 2016 to October 2018, 48 of them were performing elective surgery and 32 from emergency, clinically evident AL occurred in twelve patients (15%). Five of those were admitted from emergency while seven of them were performing elective surgery (Table 1).

Author performed this study at 50 male and 30 female patients. From 50 male patients, 8 patients developed AL percentage of 16%, while four female patients from 30 developed AL by percentage of 13.3%. The mean age was 49.1±15.15 while median age was 46 years range (17-75) years (Table 1).

Anastomotic leakage was diagnosed on median day 6 (range, 5-7) and all occurred before discharge from hospital. Twelve patients were urgently re-operated on 6 patients had simple loop ileostomy, other 6 patients had double barrel colostomy. Wound infection was significantly higher in anastomotic leakage group 10 from 12 patients (83.3%) versus 8 from 68 patients (11.8%) in patients without anastomotic leakage (p value 0.001).

Table 1: Comparison between the studied groups according to demographic data.

Variables		No anastomotic leakage (n=68)		With anastomotic leakage (n=12)		P value
Type of admission	Elective	41	60.3%	7	58%	0.824
	Emergency	27	39.7%	5	42%	
Age		46.97±15.15		62.83±8.11		0.018
Sex	Male	42	61.8%	8	66.7%	0.819
	Female	26	38.2%	4	33.3%	
BMI		27.29±2.39		28.63±2.55		0.216
Intoxication	No	48	70.6%	6	50%	0.321
	Yes	20	29.4%	6	50%	
ASA	I	30	44.1%	0	0.0%	0.005
	II	34	50%	6	50%	
	III	4	5.9%	6	50%	
Neo adjuvant treatment	No	66	97.1%	10	83.3%	0.155
	Yes	2	2.9%	2	16.7%	
Hospital stay		6.76±0.78		12.17±1.60		0.001
Wound infection	No	60	88.2%	2	16.7%	0.001
	Yes	8	11.8%	10	83.3%	
Leak day				6.17±0.41		

BMI: Body mass index, ASA: American Society of Anesthesia scale.

The hospital stay for the patients with anastomotic leakage was 12.17±1.6 days (10-14), which took significantly longer than those without AL, at 6.76±0.78 days (6-9) (p value 0.001) (Table 1).

In this study, colon leakage score was considered positive when a score of more than 11 points was recorded during the primary admission (preoperative and intraoperative). Number of patients with positive score 14 about 17.5% while there were 66 patients with negative score about 82.5%. Total sensitivity was 66.7%, total specificity was 91%, accuracy about 87.5%, total positive predictive value was 57%, and total negative predictive value was 94%. In this study, DULK score was considered positive when a score of more than three points was recorded on any time during the primary admission. Number of patients with positive score was 18 about 22.5% while there were 62 patients with negative score about 77.5% (p value <0.001) (Table 2).

Table 2: Comparison between the studied groups according to Dutch score at 4th and 5th postoperative day.

DS4 and DS5	A L				P
	Without leakage (n=68)		With leakage (N=12)		
	N	%	N	%	
Negative	62	91.2%	2	16.7%	<0.001
Positive	6	8.8%	10	83.3%	

AL: anastomotic leakage, N: Number, P: P value, DS4 & DS5: Dutch score at 4th and 5th postoperative day.

Total sensitivity was 83.3%, total specificity was 88.2%, accuracy about 87.5%, total positive predictive value was

55.6% and total negative predictive value was 96.8%. *E. coli*, *E. faecalis*, *Klebsiella*, and *Bacteroid* micro-organism were significantly more in AL group in first, third, fifth days postoperatively. *E. coli* was the most common micro-organism detected in patients with AL. In this study, a cut-off value of 120 mg/l on POD, 3 maximized the sensitivity (83%) and specificity (94%) and a positive predictive value (71.4%) and a negative predictive value (97%) of serum CRP in predicting the risk of leakage. In the postoperative period, it was clearly observed that from POD 2 onwards, the values of serum CRP were significantly higher in anastomotic leakage group. In group without anastomotic leakage, mean serum CRP reached a peak on POD 2, followed by a rapid decline thereafter (p value 0.001) (Table 3). In this study, mortality rate was 0%.

Table 3: Comparison between the studied groups according to C-reactive protein at third postoperative day.

C-RP (POD3)	AL				P
	Without leakage (n=68)		With leakage (n=12)		
	N	%	N	%	
Negative	64	94.1%	2	16.7%	<0.001
Positive	4	5.9%	10	83.3%	

C-RP (POD3): c-reactive protein at third post-operative day.

DISCUSSION

AL was defined as the existence of peritonitis during reoperation, discharge of fecaloid content through a drain tube or surgical wound, contrast extravasation seen on a barium enema test, or presence of air or a collection in an area close to the anastomosis, as detected by computed tomography scan. Minor (Clavien-Dindo I-II) was defined as leaks that did not require any therapeutic intervention, while major leaks (Clavien-Dindo III-V) required percutaneous drainage or reoperation.[7]

The overall percentage of leakage in this study was 15%. Other studies showed wide difference in leakage rate. The original study of Dulk et al, showed 9.4% AL rate less than this tudy.[4] The study of Kostas et al, showed anastomotic leaks occur as same as this study in approximately 15% of patients undergoing colorectal surgery.[8]

Buchs et al, study showed that leak rate higher than this study reached up to (39%).[9] Konishi and his colleagues reported that the overall incidence of colorectal AL, ranging from 0.5% to 30%.[10] Komen et al, reported that leakage rate varying between 2 and 24%.[1]

This study showed that the incidence of AL was correlated with higher age, with mean age of leak group 62.83 years and (p value 0.018). These results are in keeping with a study by survey of the Italian Society of Colorectal Surgery that included a group of 520 patients who had undergone a low anterior resection were evaluated. The incidence of AL was correlated with higher age, with mean age of leak group 68.6 years and (p value 0.014).[11] Similar results obtained from a study by Jung et al, old age was significant risk factor (p value 0.021).[12]

This study found that male gender was a risk factor for leakage. Most likely, gender only influences low anastomoses, where the narrower male pelvis makes dissection and anastomoses more challenging.[13] In a prospectively evaluated cohort of male patients, Branagan et al, noted that there was a substantially higher rate of leakage in male (5.6%) compared with female patients (2.4%) throughout the colon and rectum.[14] Lipska et al, found the same result, as regard male sex being a risk factor.[15]

This study showed no statistical difference between elective and emergent anastomosis as regard leakage development (p value 0.824). However, Choy et al, identified emergency procedures as a significant risk factor for anastomotic leak.[16]

Also Choi et al, advocated that the emergency intervention was the most significant factor associated with anastomotic leakage as surgery performed in an emergency setting, on debilitated patients without adequate preoperative preparation and stabilization, has an increased risk for anastomotic dehiscence.[17]

In this study, according to Dulk score, total positive predictive value was 55.6% and this also a relatively higher value compared to study of Martin et al, which had a total positive predictive value 22% and the study of Dulk and his colleagues which showed positive predictive value of 16.2%.

Original study of Dulk et al, showed negative predictive value of 99.5% while negative predictive value at this study was 96.8% which is slightly less than negative predictive value at Martin and his colleagues which was 98%. Total sensitivity was 83.3% at this study slightly smaller ratio when compared by a sensitivity of 91.67% at Martin et al, study, both of those are less than sensitivity of original study of Dulk et al, which is 97%.

This study had a specificity of 88.2% which is higher than specificity at Martin G et al. study which was 55.6% and both of them are higher than specificity of Dulk et al, which is 53.6%. At this study, the median interval between appearance of the initial signs of clinical deterioration i.e. a DULK-score >3 and the confirmation of AL was three days While at the study of Martin G et al, it was more helpful as it permitted diagnosis of anastomotic leak three and half days earlier.[18]

In this study, a cut-off value of 120 mg/l on POD 3 maximized the sensitivity (83%) and specificity (94%) and a positive predictive value (71.4%) and a negative predictive value (97%) of serum CRP in predicting the risk of leakage ($p < 0.001$).

In the study of Warchkow et al, concluded that the cut-off point that they established on the fourth day of the postoperative period was 135 mg/l, with an NPV of 89%, 68% sensitivity and 83% specificity.[19] Platt et al observed that, on post-op day 3 and with a cut-off point of 190 mg/l, sensitivity was 77% and specificity 80%, meanwhile, on day 4 and with a cut-off point of 125 mg/l, sensitivity was 77% and specificity 76%.[20]

While Ortega-Deballon et al, published an article in which they considered CRP was a useful predictor to detect AL on day 4, since the sensitivity 81.8%, specificity 64.4% and the NPV 95.8% for a CRP cut-off point of 125 mg/l.[21]

Singh et al, concluded that the best day is the POD4 with a cut-off point of 124 mg/l, which obtained an NPV of 97%, a PPV of 21%.[22] Fernandez et al, observed that CRP was useful on postoperative days 4 with cut-off point of 159.2 mg/l, sensitivity 75%, specificity 89% and NPP 96%.[23]

In this study, revealed mortality rate 0%. The study of Dulk et al, showed 24% AL associated mortality.[4] While other study revealed mortality ranges between 10 and

50%.[8] Martin et al, revealed mortality rate of about 17%.[18] Therefore, the principle of this study was not to force surgical intervention but to alert the care-takers of the risk of AL and then to intensify surveillance and prescription of the necessary additional investigations leading to early diagnosis.

Thus, DULK-score has a major role in risk management and ‘‘failure to rescue’’ reduction. Its value is to improve risk management in GI surgery with the intent of reducing associated mortality by earlier, more reliable diagnosis of AL during early post-operative days. Routine application of DULK-score leads to a diagnosis of AL three days earlier. C-reactive protein is a simple way to ensure a safe discharge from hospital after colorectal surgery. Patients with CRP values >120 mg/l on the third postoperative day should not be discharged.

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