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COLORECTAL ANASTOMOTIC LEAK – UNEXPECTED FATAL DISASTER OR A PREDICTABLE CONTROLLED PROBABILITY? A 2009 UPDATE.

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ABSTRACT

Despite improvements in surgical technique, anastomotic leakage/AL/ after colorectal cancer surgery/CRCS/ continues to be a major clinical problem with high mortality and morbidity, hospital resources and costs and worse oncological prognosis. Assessing risk factors, early clinical signs and symptoms of an AL using modern diagnostics earlier either only conservative or most oftenly operative treatment must be performed.

We studied retrospectively for 12 years period /1998 to 2008/ 404 patients with CRC who underwent primary resections and anastomoses. Patient related variables supposed to act as risk factors for anastomosis leakage like gender, age, comorbid disease, ASA score, site of tumor, bowel preparation, timing and mode of operation and drainage were thoroughly analyzed. Type of different operation was compared in relation to leak occurrence as well as morbidity and mortality rates. AL was considered to be present when described atrelaparotomy or endoscopy, or when post-operative computerized tomography scan showed the presence of air or fluid collections or an infiltrate surrounding the anastomosis. Leaks occurred between the 5th and the 15th postoperative days, with the onset of abscess, peritonitis or systemic sepsis. There were 10 AL /2.5%/ related more to rectum/4/ and sigma/2/ resection/anastomosis. AL in the early stage of localized peritonitis, with minor defect are oversewed and drained or reresection with proximal diverting stoma performed. In advanced diffuse peritonitis either obstructive resection or exteriorization has been applied. Thorough analysis of risk factors is extensively discussed and conclusions on improving rates and outcome of AL after CRCS are outlined.

Key Words: Anastomosis leakage/AL/, Colorectal Cancer Surgery/CRCS/

INTRODUCTION

Despite improvements in surgical technique, anastomotic leakage/AL/ after colorectal cancer surgery/CRCS/ continues to be a major clinical problem/1,2,3/.

It is feared and dreaded complication associated with early and long-term morbidity and mortality, prolonged postoperative length of stay and considerable demand for hospital resources and costs /4,5, 6/.

Anastomotic dehiscence occurs more commonly in rectal anastomoses than in anastomoses of the other parts of the alimentary tract. Due to technical diffi culties in accessing this area and its easily compromised blood supply/7/.

The reported leak rate varies between 1% and 39% depending on the definition of a leak, and type of resection, although experienced colorectal surgeons often quote 3% to 6% as an acceptable overall leakage rate/ 1,3, 4, 5, 8, 9/.

The incidence of clinically significant leakage after low anterior resection (LAR) varies between 3% and 21%,but is thought to average 10%. Or lower when patients are operated by a high-volume surgeon /7,9/

Postoperative mortality rates following an anastomotic leak may be as high as 39% 1,4,7 Identifying a leak as early as possible can reduce the morbidity and mortality rates and improve outcomes/1/.

There is no uniformly accepted definition of an AL in the literature, because more than 56 different definitions were describedIn 1991,the United Kingdom Surgical Infection Study Group proposed the definition as a "leak of luminal contents from a surgical join between two hollow viscera."/4/. AL is defined as the breakdown of a colonic anastomosis associated with an intraabdominalcollection identified either by contrast radiographs before a subsequent operation or by the surgeon at the time of a subsequent operation/10/.

A clinical AL was described as the presence of luminal contents through a drain or wound site or abscess cavity causing inflammation (ie, fever, leukocytosis, or fecal discharge/6/ or a clinically apparent leakage sign(such as emission of gas pus or feces from thre pelvic drain or peritonitis) or extravasation of an endoluminaly administered water soliable contrast medium according to computed tomography early postoperatively /11/.

Free AL is featured by free perforation and associated peritonitis, while contained AL are with presence of localized findings on contrast radiographs and lack of peritonitis/10/.

Risk factors can be categorized as patient-specific, intraoperative, and specific for low rectal anastomosis. Table No 1/4,9/.

Table 1 Modified categorization of risk factors for AL.

Patient factors	Malnutrition, BMI, advanced age Steroids, statins Tobacco and alchohol use, Leukocytosis, ASA score, Cardiovascular disease, Diabetes Diverticulitis
Disease related factors	Type of neoadjuvant therapy Radio- or chemotherapy or a combination
Operative and Surgeon related factors	Urgent vs elective operation Mechanical bowel preparation Perioperative blood transfusion Low anastomosis > 7sm from anus Peritonitis, Ileus Worsen blood supply to anastomosis Anastomosis configuration Surgeon or assistant Operative time >2 hours, night hours
Specific factors for low anastomosis	Male Obesity

AIM

The aim of this retrospective study was to identify the mode of presentation of patients with a clinical AL following CRCS in order to facilitate early diagnosis and treatment.

MATERIALS AND METHODS

We studied retrospectively all cases of resections and anastomoses for colorectal cancer in our clinic, from 1998 to 2008. For 12 years period 748 patients have been operated in our clinic for different localizations of colorectal cancer, 404 of whom underwent primary CRC resections and anastomoses. Patient related variables supposed to act as risk factors for anastomosis leakage like gender, age, comorbid disease, ASA score, site of tumor, bowel preparation, timing and mode of operation and drainage were thoroughly analyzed./Table No2/ Type of different operation was compared in relation to leak occurrence as well as morbidity and mortality rates.

Table No 2 Patient variables and tumor localization in AL after CRCS

Characteristic	Leak	No leak
Age	67.5/50 -91/	59.2/41-89/
Gender M/F	7/3	209/185
ASA score	I:1, II:4,III:4,IV:1	I:3,II:110,III:185,IV:96
Co-morbid disease > 1	10	
Site of CRC No of Patients	10	394
Ca coeci	-	52
Ca colonis ascendens	1	57
Ca flexura hepatica	1	30
Ca colonis transversi	2	15
Ca flexura lienalis	-	20
Ca colonis descendens	-	18
Ca sigmatis	2	93
Ca rectosigmoidalis	-	12
Ca recti	4	95
Multiple Ca	-	2
Urgent vs. elective	Urgent 6, Elective 4	Urgent 41 Elective 353
Stapled vs handsewn	Stapled 4, Handsewn 6	Stapled 108, Hadsewn 286
Prophilactic drainage	10	394
Mechanical bowel preparation	Yes 4, No 6	Yes 353 No 41
Operative time > 2 hours	10	352

RESULTS

Mean age of the patients with AL was 67.5 years/ 50-91/, while those with no leak were 59.2/41-89/. Al was observed in 7 men and 3 women. AL occurred in ASA I – 1, ASA II – 4, ASA III - 4 и ASA IV – 1 patients. More than 1 comorbid disease like diabetes, cardiovascular or pulmonary disease was present in all 10 patients with AL. Leakage of anastomosis was clinically registered in 1 patient with cancer of ascending colon, 1 of the hepatic flexura,, 2 of the transverse colon, 2 of the sigma and 4 of the rectum/Table No 3/. AL appeared in 6 urgent and 4 elective operations; 4 anastomoses with AL were stapled, 6 – handsewn. In all cases of AL operative time was more than 2 hours. Mechanical bowel preparation was done in 4 patients with leakage, in 6 – it was not performed. All of the patients with anastomosis leakage did have intraabdominal drain.

Table No 3 Types of resections and anastomoses performed for CRC included in the study

Operation Type	Leak	No leak
Right Hemicolectomy	2	119
Transverse Colon Resection	1	23
Left Hemicolectomy	1	42
Sygma Resection	2	107
Anterior Rectum Resection	4	101
Subtotal Colectomy	-	2
Total	10	404

The following postoperative complications have been registered: wound infection - 76/18.8%/, bronchopneumonia – 2 /0.5%/, embolia – 2 /0.5%/, anastomosis dehiscence – 10 /2.5%/, eventrations – 3 /0.7%/, postoperative ileus – 8 /1.2%/, postoperative hemorrhage – 4 /1.0%/, pneumothorax – 1 /0.2%/. Readmission rate was 3.5%/14/ and lethality – 4.5%/18 /.

AL was considered to be present when described at relaparotomy or endoscopy, or when post-operative computerized tomography scan showed the presence of air or fluid collections or an infiltrate surrounding the anastomosis.

Leaks occurred between the 5th and the 15th postoperative days, with the onset of abscess, peritonitis or systemic sepsis. Traditional late signs and symptoms of a leak include fever, elevated white blood cell count (WBC), gas or faecal discharge from the incisional wound, vagina or drain tract, and peritonitis /TableNo 4/. Three of the patients with AL reoperated died – 2 from severe sepsis and one polyorgan insufficiency.

Table No 4 Basic signs and symptoms of AL

Clinical signs	Pain, peritonitis, feculent or purulent discharge
Biochemical markers	Fever, achycardia, leucocitosis
Radiological studies	Fluid collection
Intraoperative findings	Gross enteric spillage Anastomotic disruption

Mean hospital stay for AL patients was was – 25.6 days. /14 – 119/.

DISCUSSION

Many risk factors have been attributed to anastomotic leakage /4/. The major surgical factors that influence the likelihood of anastomotic leakage are tension-free anastomosis and sufficient blood supply; other possible factors include age, sex, preoperative medical disease, obesity, chemoradiotherapy/CRT/, bowel obstruction, tumor location, and pelvic drainage, level of anastomosis, TME /8,11/ .

Obesity is a risk factor, because of tension and ischemia caused by a short, thick mesentery/4/. BMI higher than 30 increase the risk for developing leakage almost three-fold/9/. Tobacco and alcohol use are risk factors for anastomotic leaks mainly by causing tissue hypoxia, which compromises healing. /4,7/ Comorbid conditions, such as diabetes mellitus, hypertension, and cardiac disease all represent conditions that affect ASA status and can cause impaired circulation at the microcirculation required for a healthy anastomosis/4/.

Steroid and statins use is considered a risk factor for anastomotic leak/4/.

Preoperative CRT of only two fi elds with high doses per fraction and a small interval between fractions leads to higher anastomotic leakage rate than four-fi eld RT /4,7/. Male sex is considered a risk factor for leakage, due to the narrow male pelvis which makes low anastomoses technically more demanding as a result of poor visualization during

dissection/4,7/. In our patients with leakage 7 were men, while only three – women. Hypoalbuminemia or low prealbumin levels places a patient at higher risk for anastomotic leaks. Albumin value lower than 30 g/dl and recent weight loss of more than 5 kg are risk factors for leakage/4,7/. Perioperative blood transfusions induce immunosuppression predisposing to various postoperative infections, therefore increasing the risk of anastomotic leakage/7/. Patients with leakage had a significantly lower collagenI/III ratio and higher expression of metalloproteasis than patients without leakage/7/. Bevacizumab, a monoclonal antibody, targeting the vascular endothelial growth factor receptor can cause perforation due to arterial microthromboembolic disease leading to bowel ischemia/4/. The incidence of leakage is increased during celecoxib /cyclo-oxygenase inhibitor/ for postoperative analgesia use/12/.

Patients with leakage had lower tissue oxygen saturation at the anastomosis site than patients without anastomotic leakage. Ligation of the inferior mesenteric artery at its origin (high ligation) may severely compromise the blood supply of the sigmoid colon, because the division is proximal to the origin of the left colic artery. The peritonealization of the pelvis and the extraperitoneal positioning of the anastomosis reduces the occurrence of peritonitis after anastomotic leakage /7/. We have always tried to extraperitonize low rectal anastomosis .The global clinical risk assessment of anastomotic leakage by the operating surgeon has low predictive value for anastomotic leakage and underestimates the risk of anastomotic leakage/3/. Duration of operations more than 2-4 hours has higher leak rate, associated with more difficult resections and anastomoses. All of our AL appered after operation lasting more than 2 hours.

Tissue ischemia at the site of the anastomosis is frequently cited and implicated as a cause for anastomotic breakdown. Laser Doppler scans before and after mobilizing, dividing, and anastomosing the colon show a 32% reduction in colonic tissue perfusion 2 cm proximal to the anastomotic site and a 51% decrease at the anastomotic site. Location of the vascular ligation has no impact on colonic perfusion, but location of the resection is vital to tissue oxygenation. Proximal lumen of the bowel must always be inspected. If the mucosa is pink then the blood supply is adequate. Relying on merely looking at the serosal surface is fraught with pitfalls, as the serosa might be viable but the mucosa is not/4/. The leakage rate after resection of the transverse colon is remarkably high, possibly by the involvement of the watershed area at the splenic flexure and Griffiths' critical point (insufficient marginal artery at splenic flexure) contribute to this high leakage rate /9/. Omental wraps around colonic anastomoses were not justified/4/. Our policy is to mobilize the splenic flexure always when we suspect tension of the colorectal anastomosis.

Patients operated upon after-hours had more than a twofold increased risk of anastomotic leakage significantly more anastomoses were constructed by residents after-hours (95%) decreased technical performance of the operating team has contributed to a higher leakage rate at night. Medical errors to occur more often at night. In addition, physicians appear to be less proficient at night, which leads to more errors at night than during daytime . Decreased non-technical skills of the operating team at night, like teamwork- and management skills and situational awareness, contribute to higher leakage rates. Situational awareness (SA), defined as the ability of the surgeon to observe, understand and predict events in the operating room (OR), appears to be closely related to technical error rates/9/. Although we have not analyzed the urgent operations at night we believe that resections and anastomoses performed at night even by an experienced surgeon are disadvantageous and bare a risk for AL. Surgeons experiencing leak rates that exceed 3.0% should probably undergo peer review. clearly articulated definition for colonic anastomotic leaks and their expected rates from which we can benchmark surgeon performance /10/.

. A diagnostic test which measures microperfusion before and after creation of an anastomosis like visible light spectroscopy and multispectral fluorescence imaging techniques to evaluate realtime microperfusion in gastrointestinal surgery will be most suitable/3/.

The issue of routine drainage of colonic anastomoses has been a topic of controversy for years. Those championing the use of these drains believe they play a role in evacuating perianastomotic fluid collections, lessening the incidence of abscess formation and serving as an early warning marker for anastomotic dehiscence /4/. The rationale behind the placement of a drain after LAR is to promote adequate drainage of the pelvis and prevent the formation of a hematoma, which may become infected and result in a pelvic abscess, which in turn can erode the anastomosis. The pelvic drain serves as “an eye” into the pelvis, often allowing for early recognition of otherwise silent leakage of feces, pus, or air/7/. It also makes conservative treatment of a leakage feasible by creating a tract that can turn into a fecal fi stula during the postoperative period. the need for surgical reintervention after leakage was signifi cantly lower for patients with pre-existing pelvic drainage than for patients without drainage/3,13/. Although prophylactic drainage (PD) is associated with AL, suggesting that it is a risk factor./9/it may assist in its management/7/. We have always routinely used presacral tube drain, after extraperitonizing the low colorectal anastomosis, thus when AL appear, it drains the perirectal extraperitoneal splittage, preventing from peritonitis.

Given the wide array of results in the literature that has examined the use of a bowel prep, mechanical preparation is recommended to minimize contamination /4/, although some state that bowel preparation is not necessary even after TME for rectal cancer /7/. In elective CRCS since 3 years we have started a protocol based study avoiding mechanical bowel preparation.

There is strong evidence that rates are equal from a multicenter, randomized, prospective trial comparing handsewn to stapled anastomosis in elective and emergent colorectal operations not a statistically significant difference even with low anastomoses /4/ The lower-lying anastomoses require more stapling devices. The learning curve for the stapling devices has not been fully evaluated, but it is thought to be less steep than that for manually constructed anastomosis/7/. AL in our stapled anastomoses were 4 , while in hand sewn they were 6. We perform stapled colorectal anastomoses since 1993 and having much experience both with circular and linear stapler colorectal anastomoses recommend them as superior to handsewn, not only for low anterior rectum resection.

Leak rates of 7% above the peritoneal reflection are compared with 18% 5 cm from the anal verge /4,7/. From a study of 1014 stapled anastomoses AL above 7 sm from the anal verge was 1%, while below 7 sm It was 7.7% /11/. From 10 CRCS leaks we have had 4 after low rectal resections and 2 after sigma resections, which implies that low rectum resections are more amendable to AL.

A defunctioning stoma decreases clinical anastomotic leak rate and reoperation rate and is recommended after low anterior resection for rectal cancer/14/. Proximal diversion does not prevent leaks, but lessens the dreaded sequelae should a clinical leak occur, even in higher-risk patients. Stomas are not without inherent complications of their own, such as necrosis, retraction, prolapse, and disuse stricture of a distal anastomosis /4/. The argument against the use of protective stomas is overtreatment. reconstruction is an additional operation/7/We have never performed primary diverting stoma in our 404 CRC primary resections and anastomoses.

A method of reducing the potential for anastomotic leak is intraoperative testing of the integrity of the anastomosis with isotonic sodium chloride solution, povidone-iodine, or air insufflation of the anastomosis. However, others suggest that the results of leak testing may influence the decision to perform additional exploratory surgery in a patient in critical condition. Because the knowledge of a sound anastomosis at intraoperative testing provides a

false sense of anastomotic integrity untested anastomoses have twice the rate of postoperative clinical leaks compared with those that were tested. An airtight anastomosis at intraoperative testing is a reliable indicator of anastomotic integrity /7/

AL are detected from 3 to 45 days postoperatively. When leaks occur clinically, the median postoperative day of diagnosis is 7 days; when made radiographically the median postoperative day of leakage is 16/4/. Diagnosing leaks relies on the clinical picture and radiographic findings. The earliest predictors of an anastomotic leak are respiratory and neurological in nature. /1/.

Prompt an early work-up to rule out the development of an anastomotic leak and reduce morbidity and mortality associated with this complication. Tracking resource utilization and outcomes in the setting of a prospective study with standardized cardiac, respiratory and neurological preoperative assessmentand monitoring helps to identify and treat leaks earlier. Computed tomography (CT) is the most readily available imaging tool for diagnosis of postoperative lower gastrointestinal tract (LGIT) leak. CT studies on patients shortly after abdominal surgery are not definitive. A negative CT study does not rule out LGIT leak. Clinically based decision making and exploratory relaparotomy still do play a role in those patients withsuspicion for LGIT leak. /15/

Patients with anastomotic leaks most often require volume resuscitation and should all be started on broad spectrum antibiotics. Once an anastomotic leak has been recognized, management should be individualized to accommodate patient's needs/4/. Patients with contained leaks tend to be treated with percutaneous drainage, whereas the patients with free leaks tend to be treated surgically with emergent reexploration, takedown of the anastomosis and creation of an end stoma, or a proximal diversion via a loop ileostomy/10,16/.

Available strategies include observation and bowel rest, percutaneous drainage, colonic stenting, and surgical revision, diversion, or drainage. With a small degree of contamination, right-sided colonic leaks can often be reanastomosed and drained. With more extensive contamination, resection with ileostomy and mucous fistula or creation of a Hartman's pouch should be used/4,6/. Management of left-colon leaks depends on the level of the anastomosis. Intraperitoneal leaks should be resected with the ends brought out as ostomies, if possible. Extremely low anastomotic leaks should be extensively drained with proximal complete diversion with either an ileostomy or colostomy. Newer approaches use endostents and transanal endoscopic vacuum devices. /4/

From 4019 colorectal resections and primary anastomoses /1992 – 2004 / with 58 AL /largest series of symptomatic leaks in the literature/ Damrauer and aut. suggest that the differences between free and contained leaks may be a result of wishful thinking more than of actual clinical outcomes/10/. Contained leaks tended to have the same signs and symptoms as free leaks. Although they were more likely to have been subjected to attempts at nonoperative treatment, this modality failed in almost all patients with contained leaks, and these patients subsequently required surgical intervention/10/.

When AL is in the early stage of localized peritonitis, with minor defect we oversew and drain it,.or do reresection with proximal diverting stoma. In advanced diffuse peritonitis we perform either obstructive resection or exteriorization.

Tumor cells present in the colonic lumen after resection that can implant and grow in the remaining colorectal segment. anastomotic leak is independently associated with worse longterm outcomes. Iintraluminal tumor cells that are normally inconsequential after a colon resection may implant after a leak. A third option is these patients might have decreased immune function from morbidity associated with a leak /4/. AL have significantly poorer long-term survival/11/.

Preventing AL is offered by various types of nonabsorbable, semiabsorbable, and absorbable material to buttress staple lines to strengthen anastomoses/6/; intraluminal tubes such as the

SBS tube (absorbable) and the Coloshield (permanent); endo-sponge device/5/ sealing colon anastomoses with fibrin, but there is little evidence to support its widespread use currently /4/.

Table No 5 Current status of risk factors for anastomosis leakage in CRCS

Facts	Obscurity	Fiction
Risk Factors	Collagen type	Tumor stage
Male sex	Enzyme expression	Stapled or hand-sewn anastomosis
Smoking, alchohol	Long RT plus ChT	Short sheme RT
Malnutrition	Blood trahsfussion	Omentoplasty
Hight of anastomosis		Extraperitoneal anastomosis
Splenic Fl mobilization		Bowel preparation
BMI >30kgm2		
After hours operation		
Protective measures		
J-pouch	Protective stoma	Pelvic drains

Currently available risk estimating systems have one or more limitations associated with lack of specificity to operation type, size of sample (reliability), range of outcomes predicted, and appreciation of hospital effects. The ACS colorectal risk calculator allows surgeons to preoperatively provide patients with detailed information about their personal risks of overall morbidity, serious morbidity, and mortality /17/. Sequelae of colon and rectal anastomotic leaks are substantial. Mortality rates range from 0% to 32%./14,18/.

CONCLUSION

Because of the substantial morbidity and mortality associated with delayed recognition, detection and investigation of an anastomotic leak, it is imperative to diagnose and treat this complication as early as possible.

Treatment of a colonic anastomotic leak must then be individualized to the location and sequelae of the leak. Treatments range from nonoperative percutaneous drainage to surgical revision or resection of the anastomosis.

Although there is ongoing research into new technological methods to prevent anastomotic leaks, no currently available methods have been widely accepted.

Now in the ongoing 2009 AL after CRCS, though a major surgical problem with medical and social impact on quality of surgical care and patient life, has lowered its rate to the acceptable 3 % in specialized centers, mainly due to surgeons experience and technical proficiency, modern diagnostics and risk assessment, turning out from an embarrassing fatal disaster in the past to a predictable probability today and hope in the future.

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