

ANASTOMOTIC FISTULAS FOLLOWING SURGERY FOR COLO-RECTAL CANCER – 6 - YEAR RETROSPECTIVE STUDY

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Abstract: Anastomotic leaks are the most serious complication of colo-rectal surgery, generating significant morbidity and mortality rates. We performed a 6-year retrospective study in which we included patients who developed anastomotic colo-rectal fistulas after resections for malignant disease. We assessed the risk factors for this complication, its management and results. Twenty-two patients aged between 34 and 82 years were enrolled, with an equal number of males and females (11). Following the surgical procedures, 4 types of anastomotic leaks resulted: ileo-colic (6 cases), colo-colic (8 cases), colo-rectal (5 cases) and low colo-rectal (3 cases). Conservative management was applied for 10 patients while the other 12 required surgical treatment. The overall mortality of this study group was 13.6%. Better optimisation of surgical procedures and preoperative patients' comorbidities might decrease the rate of this complication. Therapeutic management is not standardised but adapted to each patient's condition, but conservatory management should be initiated to all eligible patients.

INTRODUCTION

Despite a large number of studies performed in the latest years and progress in diagnosis and therapy, the anastomotic fistula remains one of the most feared postoperative complications following colo-rectal surgery. It generates significant morbidity and mortality rates, prolongs the length of hospitalisation thus increasing the costs and can alter the oncological outcome of the patients.⁽¹⁾ The incidence of the colo-rectal anastomotic fistula varies between 5 and 30% (1-7) with a mortality rate between 2 and 25% reported in large studies.^(1, 8-13) Both patient-related and operative-related risk factors have been described.^(1,14) The management of the anastomotic leaks is individualised to each patient, depending on their general status. Although in the past, surgery was mandatory for this pathology, the conservative treatment could be successful for patients with good condition.^(8,12,14-16)

PURPOSE

The article presents an analysis of the diagnosis, risk factors and therapeutic approach of the anastomotic leaks following colo-rectal surgery for malignant pathology performed in our clinic.

MATERIALS AND METHODS

We performed a 6 year (January 2013 – December 2018) retrospective, single-center, study in which we included patients who developed anastomotic colo-rectal fistulas. All patients were treated in the General Surgery Department of “Bagdasar – Arseni” Emergency Hospital. During this period, 297 rectal and colonic resections for cancer were performed, for which multiple types of ileo-colo-rectal anastomosis were made in 142 of these cases. We have selected only patients aged 18 or more, who developed external digestive fistulas after colo-rectal resections for cancer, followed by an anastomosis. We have also included patients with ostomies made for complicated colo-rectal tumours who were admitted and operated for stoma

reversal that was complicated with anastomotic leaks. The fistulas were diagnosed either by clinical findings or by imaging studies (extravasation of contrast substance during contrast enema or CT evidence of an abscess formed at the site of the anastomosis). Patients with internal fistulas (recto-vaginal, recto-vesical), multiple fistulas (involvement of more than one segment of the digestive tract), the ones produced by drain tube lesions or after surgeries for benign diseases were excluded. In the end, 22 patients (15.49%) were enrolled in our study.

We analyzed the patients' age and sex distribution, the stage of the malignant tumours according to TNM classification, and whether the surgery was performed in emergency or elective conditions. We identified the patient-related risk factors: malnutrition – loss of more than 10% of body weight in less than 2 months, arterial hypertension > stage II, ischemic cardiopathy or cardiac insufficiency > class II NYHA, diabetes with HbA1c > 7,5%, history of smoking more than 10 packs – year, anaemia – Hb < 11 g/dl, hypoalbuminemia < 3,5 g/dl. Also, the operative-related risk factors were assessed: the surgical procedure, the suture type performed (mechanical or manual), the operative time, intraoperative hypotension – systolic arterial pressure less than 90 mmHg for more than 15 consecutive minutes and the intraoperative blood losses. We have also studied the time between surgery and fistula onset, the therapeutic management and the results, with the primary endpoint being the overall survival. All data was obtained from the patients' hospital records.

RESULTS

A number of 22 patients aged between 34 and 82 years (mean age: 65.7 years) were included in our study. Eighteen of them were older than 60 years. The gender distribution was balanced, with an equal number of males and females (11:11). Regarding the stage of colo-rectal cancer at the moment of the surgery, 10 patients had stage II, 10 stage III, 2 stage IV of the disease, and none of the patients was in the first stage (table no.

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CLINICAL ASPECTS

1).

Table no. 1. Stage of the malignant disease

Stage of cancer	Number of patients
Stage I	0 (0%)
Stage II	10 (45.45%)
Stage III	10 (45.45%)
Stage IV	2 (9.01%)

Surgical procedures

The surgical procedures after which anastomotic fistula developed are presented in table no. 2. For 6 patients right hemicolectomy was performed, 5 underwent segmental resection of the sigmoid, 4 had left hemicolectomy, 4 anterior colo-rectal resections and 3 patients were operated for stoma reversal. In all cases we performed a digestive anastomosis (ileo-colic, colo-colic or recto-colic), 8 of which were manual sutured. For the other 14, a mechanical anastomosis was made using either linear staplers or transanal circular staplers. Two procedures were made in emergency conditions for tumours located at the hepatic flexure of the colon – one complicated with stenosis and bowel obstruction and one with perforation, for which right hemicolectomy with ileo-colic anastomosis was performed. Mechanical bowel preparation was used for all patients with scheduled procedures and diverting stomas were never used. The operative time varied between 140 and 300 minutes, with a mean time of 198 minutes. Intraoperative hypotension was identified in 4 cases. Thirteen patients had an operative blood loss of more than 200 ml, with a mean value of 210 ml.

Table no. 2 Main characteristics of the surgical procedures complicated with anastomotic leaks

Surgical procedure	Anastomosis type	Operative time	Intraoperative blood loss	Intraoperative hypotension
Right hemicolectomy - 6 cases	Mechanical 3 Manual 3	150 – 280 min Mean: 165 min	150-250 ml Mean: 190 ml	1 case
Segmental sigmoidian resection - 5 cases	Mechanical 3 Manual 2	150-300 min Mean: 230 min	150 – 300 ml Mean: 220 ml	1 case
Left hemicolectomy - 4 cases	Mechanical 4 Manual 1	140-180 min Mean: 160 min	140 – 250 ml Mean: 195 ml	0 cases
Anterior rectal resection - 4 cases	Mechanical 4 Manual 0	200 – 300 min Mean: 245 min	250 – 300 ml Mean: 260 ml	1 case
Stoma reversal - 3 cases	Mechanical 1 Manual 2	160 – 240 min Mean: 193 min	150 – 200 ml Mean: 183 ml	1 case
Total: 22 cases	Mechanical - 14 Manual - 8	140 – 300 min Mean: 198 min	150 – 300 ml Mean: 210 ml	4 cases

Patient-related risk factors

The prevalence of patient-related risk factors in our study group is presented in table no. 3. The most frequent were hypoalbuminaemia (mean value > 2.9 g/dl) in 90.9% of the patients, arterial hypertension (68.1%), long history of smoking (54.5%) and anaemia (45.4%). We have also observed that 15 patients (68.1%) had 3 or more risk factors associated.

Table no. 3. Patient-related risk factors

Risk factors	No. of patients
Hypoalbuminemia (<3.5 g/dl)	20 (90.9%)
Arterial hypertension	15 (68.2%)
Smoking	12 (54.5%)
Anemia (<11 g/dl)	10 (45.4%)
Cardiopathy	6 (27.3%)
Diabetes	5 (22.7%)
Malnutrition	2 (9.1%)
Radiotherapy	1 (4.5%)

Postoperative care

All patients were extubated at most 6 hours after the end of the surgical procedure and were admitted in the Intensive Care Unit for at least 24 hours, where they received antibiotics, non-opioid analgesics, prokinetic treatment, non-steroidal anti-inflammatory drugs and prophylactic anticoagulation with low molecular weight heparin. Eighteen patients (81.8%) received more than 8000 ml iv fluids during the 72 hours perioperative period. Twelve patients required (54.5%) at least 1 unit of red cell concentrate transfusion. Postoperative oral feeding was resumed after a mean time of 3.5 days, ranging from 1 to 6 days, depending on the patients status and bowel movement.

Fistula characteristics

Following the surgical interventions 4 types of anastomotic leaks resulted (table no. 4): ileo-colic (6 cases), colo-colic (8 cases), colo-rectal (5 cases) and low colo-rectal (3 cases). For the majority of the patients, the fistulas were diagnosed based on the clinical evidence of external drainage of enteral content through an intraabdominal drain tube or the surgical wound. One case had a late clinical manifestation at 40 days after surgery and presented as a peritoneal abscess and another patient had a sudden cardio-respiratory dysfunction associated with signs of peritonitis. The mean time interval between surgery and anastomotic leakage onset was 8 days (range 4 to 40 days) and only one patient was diagnosed after hospital discharge.

The output of the fistula ranged between 50 and 750 ml/24h with a mean of 270 ml/day. According to enterocutaneous fistula classification by their output, 12 patients had low-output fistulas, 7 had medium-output and 4 had high-output leaks – mostly from the ileo-colic anastomosis (table no. 4).

Table no. 4. Main characteristic of the anastomotic fistulas

Type of anastomotic fistula	Fistula onset	Debit	Treatment	Result
Ileo-colic (6)	5 – 40 days Mean: 13 days	<200 ml - 1 case (16.6%) 200-500 ml - 2 cases (33.3%) >500 ml - 3 cases (50%)	Surgical - 4 (66.6%) Conservatory - 2 (33.3%)	Healed - 4 (66.6%) Deceased - 2 (33.3%)
Colo-colic (8)	4 – 11 days Mean: 6,4 days	< 200 ml - 4 cases (50%) 200-500 ml - 4 cases (50%) >500 ml - 0 cases (0%)	Surgical - 3 (37.5%) Conservatory - 5 (62.5%)	Healed - 8 (100%) Deceased - 0 (0%)
Colo-rectal (5)	4 – 7 days Mean: 5,6 days	< 200 ml - 4 cases (80%) 200-500 ml - 1 case (20%) >500 ml - 0 cases (0%)	Surgical - 2 (40%) Conservatory - 3 (60%)	Healed - 5 (100%) Deceased - 0 (0%)
Low colo-rectal (3)	5 – 6 days Mean: 5,6 days	< 200 ml - 3 case (100%) 200-500 ml - 0 cases (100%) >500 ml - 0 cases (0%)	Surgical - 1 (33.3%) Conservatory - 2 (66.6%)	Healed - 2 (66.6%) Deceased - 1 (33.3%)
Total (22)	4 – 40 days Mean: 8 days	< 200 ml - 12 cases (54.5%) 200-500 ml - 7 cases (31.8%) >500 ml - 3 cases (13.7%)	Surgical - 10 (45.4%) Conservatory - 12 (54.6%)	Healed - 19 (86.4%) Deceased - 3 (13.6%)

CLINICAL ASPECTS

Management

Conservatory treatment was applied to all patients with a good condition, who did not have peritoneal signs or sepsis and maintained a good oral food tolerance and bowel movement. It was the initial treatment of choice for all patients, except the case in which the leakage produced a sudden alteration of the general status of the patient along with peritoneal signs, requiring emergency relaparotomy. The non-operative approach consisted of broad-spectrum antibiotics, prokinetic treatment, correction of electrolytes and intravenous hydric replacement, and, in some cases, nutritional support. For one patient percutaneous CT guided drainage of a peritoneal abscess was performed. Conservatory treatment alone managed to produce spontaneous closure of the fistula in 12 patients (54.5%).

Surgery was mandatory for ten patients (45.5%) due to peritonitis, bowel obstruction and alteration of the general status or for leaks unresponsive to conservatory treatment – especially the high-output ones. For these patients anastomosis takedown and ileo- or colostomies were performed.

Outcome

All patients who were treated only non-operatively had a favourable evolution, with spontaneous closure of the fistula in a time interval ranged between 10 and 90 days (mean: 21 days). Three patients died (13.6%), all from the surgically treated group. The main cause of death was sepsis and multiple organ failure.

DISCUSSIONS

The incidence of postoperative fistula in our study group was 15.49%, similar to data from the literature.(1-7) From the gender point of view, the group was evenly balanced with the same number of males and females. Most of the patients were elder, 18 of them (81.8%) aged more than 60 years which is considered a risk factor for postoperative digestive fistulas.(17)

Increased operative time is considered a risk factor for anastomotic leaks (18-20), but the exact time limit is still debated, some considering it 120 minutes (19) and others 200 minutes.(20) All surgical procedures from our study group were longer than 120 minutes, with a mean time of 198 minutes with ten patients (45,5%) suffering surgeries longer than 200 minutes. Although intraoperative hypotension is cited as a favourable condition for fistula development (21), we have identified in our study group only 4 patients who had this condition. Significant blood loss during surgical procedure is also considered a risk factor (20, 21), but the cut-off value is still debatable – 200 (20) or 250 de ml.(21) Fifteen of our patients (68.2%) suffered an intraoperative hemorrhage greater than 200 ml, 10 (45.4%) of them even more than 250 ml, with the mean value being 210 ml.

Concerning the patient-related risk factors, more than half of our patients had hypoalbuminemia, arterial hypertension and a long history of smoking, and 45.4% had hemoglobin levels lower than 11 g/dl.

Boesen et al. showed in a study that an administration of more than 8000 ml of iv fluids during a perioperative period of 72 hours measured from the start of the procedure increases the risk of developing an anastomotic leak.(22) We also observed this fact in our group, 18 (81.8%) of the patients receiving more than 8000 ml of i.v. fluids in this perioperative period.

Most of the anastomotic leaks had a clinical onset during the fifth and eighth postoperative day, with a longer time span for ileo-colic anastomotic dehiscence. This subgroup, included the only patient that was diagnosed after hospital

discharge, 40 days after the surgical procedure. In one case the patient had a sudden alteration of his respiratory and cardiac functions along with peritoneal signs, requiring urgent relaparotomy. In the rest of the cases, the intestinal content was discharged through the operative wound or from the drain site. Except for the ileo-colic anastomotic leaks, the majority of other fistulas had a low or medium fistula output (less than 500 ml/day) and did not produce signs of sepsis, allowing an initial conservative approach. Conservatory treatment managed to produce fistula closure in 12 cases (54.5%). The mean leak output of these patients was 170 ml/day. Ten patients required surgical procedures. The indications for surgery were: peritonitis – 1 case, progressive worsening of patients' condition and biological findings – 5 cases, an altered general status associated with ileus – 2 cases and lack of favourable evolution under conservatory treatment – 2 cases. Mean output of those patients was 385 ml/day. All three deaths were from the surgically treated subgroup and were caused by the poor condition of these patients, caused by sepsis and hydric, nutritional and electrolytes disturbances. No deaths were observed in the conservatory treated subgroup.

CONCLUSIONS

Anastomotic fistulas are still the most dreadful complication of the colo-rectal surgeries, its incidents being very little reduced over the past decades, despite a great number of studies performed on this pathology. Better optimisation of surgical procedures and preoperative balance of patients' comorbidities thus eliminating most of the risk factors, might decrease the rate of this complication. Therapeutic management is not standardised but adapted to each patient's condition. Conservatory management should be initiated to all eligible patients, with great care to the inclusion criteria for this treatment, allowing for a spontaneous closure of the fistula and so avoiding another surgical procedure. Still, frequent clinical, biological and imaging reexaminations are mandatory for optimal timing of the surgeries when the conservative treatment fails.

REFERENCES

1. Basilico V, Griffa B, Radaelli F, Zanardo M, Rossi F, Caizzone A, et al. Anastomotic leakage following colorectal resection for cancer: How to define, manage and treat it. In: editors. Anastomotic leakage following colorectal resection for cancer: How to define, manage and treat it; 2014.
2. Krarup PM, Jorgensen LN, Andreassen AH, Harling H. A nationwide study on anastomotic leakage after colonic cancer surgery. *Colorectal Dis.* 2012;14(10):e661-7.
3. Vignali A, Fazio VW, Lavery IC, Milsom JW, Church JM, Hull TL, et al. Factors associated with the occurrence of leaks in stapled rectal anastomoses: a review of 1,014 patients. *J Am Coll Surg.* 1997;185(2):105-13.
4. Law WL, Choi HK, Lee YM, Ho JW, Seto CL. Anastomotic leakage is associated with poor long-term outcome in patients after curative colorectal resection for malignancy. *J Gastrointest Surg.* 2007;11(1):8-15.
5. Biondo S, Pares D, Kreisler E, Rague JM, Fraccalvieri D, Ruiz AG, et al. Anastomotic dehiscence after resection and primary anastomosis in left-sided colonic emergencies. *Dis Colon Rectum.* 2005;48(12):2272-80.
6. Vignali A, Ghirardelli L, Di Palo S, Orsenigo E, Staudacher C. Laparoscopic treatment of advanced colonic cancer: a case-matched control with open surgery. *Colorectal Dis.* 2013;15(8):944-8.
7. Basilico V, Griffa B, Castiglione N, Giacci F, Zanardo

- M,Griffa A. Anastomotic fistulas after colorectal resection for carcinoma: incidence and treatment in our recent experience. *Minerva Chir.* 2006;61(5):373-80.
8. Blumetti J, Chaudhry V, Cintron JR, Park JJ, Marecik S, Harrison JL, et al. Management of anastomotic leak: lessons learned from a large colon and rectal surgery training program. *World J Surg.* 2014;38(4):985-91.
 9. Daams F, Luyer M, Lange JF. Colorectal anastomotic leakage: aspects of prevention, detection and treatment. *World J Gastroenterol.* 2013;19(15):2293-7.
 10. Moran BJ, Heald RJ. Risk factors for, and management of anastomotic leakage in rectal surgery. *Colorectal Dis.* 2001;3(2):135-7.
 11. Rullier E, Laurent C, Garrelon JL, Michel P, Saric J, Parneix M. Risk factors for anastomotic leakage after resection of rectal cancer. *Br J Surg.* 1998;85(3):355-8.
 12. Kanellos D, Pramateftakis MG, Vrakas G, Demetriades H, Kanellos I, Mantzoros I, et al. Anastomotic leakage following low anterior resection for rectal cancer. *Tech Coloproctol.* 2010;14 Suppl 1:S35-7.
 13. Buchs NC, Gervaz P, Secic M, Bucher P, Mugnier-Konrad B, Morel P. Incidence, consequences, and risk factors for anastomotic dehiscence after colorectal surgery: a prospective monocentric study. *Int J Colorectal Dis.* 2008;23(3):265-70.
 14. Soeters PB, De Zoete JP, Dejong CH, Williams NS, Baeten CG. Colorectal surgery and anastomotic leakage. *Dig Surg.* 2002;19(2):150-5.
 15. Hedrick TL, Sawyer RG, Foley EF, Friel CM. Anastomotic leak and the loop ileostomy: friend or foe? *Dis Colon Rectum.* 2006;49(8):1167-76.
 16. Hyman N, Manchester TL, Osler T, Burns B, Cataldo PA. Anastomotic leaks after intestinal anastomosis: it's later than you think. *Ann Surg.* 2007;245(2):254-8.
 17. Munteanu I. *Fistule digestive externe postoperatorii.* Gr. T. Popa, U.M.F. Iasi; 2011.
 18. Caziuc A, Dindelegan GC, Mironiuc A. Operator-related risk factors of anastomotic leaks after colorectal surgery: an up-to-date. *Clujul Med.* 2015;88(2):124-7.
 19. Galie KL, Whitlow CB. Postoperative enterocutaneous fistula: when to reoperate and how to succeed. *Clin Colon Rectal Surg.* 2006;19(4):237-46.
 20. Telem DA, Chin EH, Nguyen SQ, Divino CM. Risk factors for anastomotic leak following colorectal surgery: a case-control study. *Arch Surg.* 2010;145(4):371-6; discussion 376.
 21. Post IL, Verheijen PM, Pronk A, Siccama I, Houweling PL. Intraoperative blood pressure changes as a risk factor for anastomotic leakage in colorectal surgery. *Int J Colorectal Dis.* 2012;27(6):765-72.
 22. Boesen AK, Maeda Y, Rorbaek Madsen M. Perioperative fluid infusion and its influence on anastomotic leakage after rectal cancer surgery: implications for prevention strategies. *Colorectal Dis.* 2013;15(9):e522-7.