Anastomotic leakage in rectal cancer surgery: incidence and risk factors

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Abstract. Background and objectives: Anastomotic leakages are major complications of colorectal cancer surgery with significant implications on patients' health, on their short-term and long-term prognosis and on health care costsas well. The aim of the study was to analyze the incidence of anastomotic fistulas and to identify the risk factors causing these complications after classic open or laparoscopic colorectal cancer surgery. Material and methods: We have performed a retrospective study of the risk factors involved in the occurrence of anastomotic leakage within the first 30 days after surgery. The study included patients hospitalized over a period of 10 years, between 2004 and 2013, and who required colon or rectal resection for neoplastic pathology, followed by anastomosis. Results: After applying the inclusion and exclusion criteria, a study group consisting of 427 patients resulted, out of which 18 had developed anastomotic leakage (4.21%). The average age of patients (p=0.639), gender (p=0.809), anemia (p=0.316), insulin-dependent diabetes mellitus (p=0.323), the type of surgery elective or emergency (p=0.775) and the type of anastomosis - mechanical or hand sewn (p=0.383) - did not statistically influence the occurrence of fistulas. The risk factor that significantly influenced the occurrence of fistulas was the stenosing, occlusive nature of the tumor [p=0.003; OR=6.805; 95%CI: 1.54-29.99)]. The incidence of anastomotic fistula depending on the type of surgery was: 8.06% (n=5) after Reybard resections, 6.25% (n=2) after left hemicolectomy, 4.23% (n=5) after right hemicolectomy, 3.5% (n=5) after Dixon operation and 1.51% (n=1) after Hartman's I procedure (dehiscence of the rectal stump). No fistulas were recorded in laparoscopic surgery. Conclusions: The stenosing nature of the tumor is the most important predicting factor for anastomotic leakage after surgery for colorectal cancer.

Key Words: anastomotic leakage, colorectal cancer

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Introduction

Anastomotic leakages are major complications of colorectal cancer surgery with significant implications on patients' health, on their short-term and long-term prognosis and on health care costs as well.

Postoperative complications and reinterventions, including those related to the colorectal cancer surgery are often considered in evaluating the quality of a surgical service. Comparison of the incidence of anastomotic fistula between various surgical services is, however, difficult to achieve because there is no uniform reporting, according to well-established criteria, so these values vary between 0 and 39% in literature.

Anastomotic fistulas were classified into three grades according to their severity (Rahbari et al 2010).

A. Small fistula without clinical manifestation, and which do not require any change in patients' management.

B. Leakage requiring active therapeutic intervention, but manageable without re-laparotomy.

C. Anastomotic leakage which requires re-laparotomy.

Identifying patients with high risk of anastomotic leakage is necessary in order to take supplementary cautions in the pre and postoperative period and to apply the optimal surgical technique adapted to the case. A diverting stoma does not influence the rate of leakage occurrence, but it may reduce its consequences and the number of reinterventions (Shiomi et al 2014).

The aim of this study was to analyze the incidence of anastomotic fistulas and to identify risk factors associated with this complication after colorectal cancer surgery, considering both classic and laparoscopic approaches.

Material and Methods

We have performed a retrospective study of the risk factors involved in the occurrence of anastomotic fistulas within the first 30 days after surgery. Patient data, tumor features and types of surgical procedure have been analyzed over the period of 10 years, between January 2004 and December 2013, in the experience of The First Surgery Clinic, from Mures Clinical County Hospital. All patients included in the study signed the informed consent form and the study was approved by the Ethics Committee of the Mures Clinical County Hospital. There have been 1155 cases of colorectal cancer operated during this period.

The study included patients aged over 18 years who required colon or rectal resection for neoplastic pathology followed by a colocolic or colorectal anastomosis. Exclusion criteria were:

patients with palliative operations (diverting stomas or internal derivations), benign pathology, reinterventions after previous colorectal surgery, transanal resections, and tumors of other origins invading the colon or rectum. A total of 427 patients were included in the final analysis. Oral mechanical bowel preparation was prescribed for all patients having elective colorectal surgery. The study included both emergency and elective operations. Anastomotic fistulas were defined as the existence of a solution of continuity between the two bowel anastomosized edges, which drains out intestinal content.

Cases suspected by anastomotic leakages upon the clinical picture (abdominal pain, fever, tachycardia, abdominal tenderness) and lab tests (leukocytosis) have been confirmed by direct visualization of exteriorized intestinal content through the wound, drain tubes or vagina, or by imaging studies (endoscopy, radiography and CT scan).

Data were collected from patient records, electronic database of the department and morphopathology department database. More variables have been analyzed to identify potential preoperative risk factors such as: gender, age, diabetes melitus, anemia with hemoglobin below 10.5g dl^{-1}, circumstances of operations (emergency or elective), type of approaches (laparoscopic or classic), type of anastomosis (hand sewn or mechanical) and type of surgical procedure. We also analyzed tumor-related factors, the presence of ascites or distant metastasis.

Statistical analysis of the data was performed using MedCalc program for statistics in biomedical research, SPSS version 17 or GRAPH Pad Prisma. We used Chi-square, Fisher, Student, Mann Whitney tests. The significance threshold widely accepted is 95% meaning p=0.05. The less the value of p is, the stronger the significance.

Results

Applying inclusion and exclusion criteria resulted in a study group consisting of 427 patients, out of which 18 had developed an anastomotic leakage (4.21% incidence). The control group of 409 patients did not develop this complication.

The average age of patients studied was 65 (65.55; min 33, max 89) years. The distribution by gender revealed a male predominance in the studied group, with a men/women ratio of 1.27/1. We found out that anemia and insulin-dependent diabetes, as preoperative variables, had no statistical significance in the occurrence of fistulas.

Univariate analysis of preoperative variables in patients with fistulas vs. patients without this complication is shown in Table 1.

Table 1. Preoperative variables in relation to fistula incidence

Variables		Fistulas (18) (4.21%)	Control (409) (95.8%)	p
Age	<65	7 (3.5%)	193	0.639
	>65	11 (4.84%)	216	
Gender	Men	11 (4.6%)	228	0.809
	Women	7 (3.72%)	181	
Anemia	Present	9 (5.77%)	147	0.316
	Absent	9 (3.32%)	262	
Diabetes with need of insulin	Present	1 (11.1%)	8	0.323
	Absent	17 (4.07%)	401	

Statistical analysis highlighted that circumstance of operation (emergency vs. elective) was not a significant factor for leakage occurrence: 4.49% in cases operated in emergency and in 4.14% after electively operations (p=0.775, OR=1.089; 95%CI: 0.349-3.395).

A percentage of 94.8% (n=405) cases have been operated by classic open approach, and no anastomotic leakage was identified in the group operated by laparoscopic approach.

In most of the cases (79.6%) hand sewn anastomosis was performed. From the total number of 18 anastomotic fistulas, 5 occurred after mechanical anastomosis: 3 cases exteriorized through the drainage tubes and 2 cases of rectovaginal fistula in patients with ultralow resection who underwent preoperative radiotherapy. The type of suture (mechanical or hand sewn) did not significantly influence the incidence of anastomotic leakage (p=0.383; OR=1.534; 95%CI: 0.531-4.426).

Types of operations that have been performed and the incidence of anastomotic leakage is shown in the next table (Table 2).

Table 2. Types of operations and leakage incidence

Procedure	Number of patients	% out of 427	% of leakage
Dixon's op.	141	33%	3.5% (n=5)
Hartmann's I op	66	15.5%	1.51% (n=1)*
Right hemicolectomy	118	27.5%	4.23% (n=5)
Left hemicolectomy	32	7.5%	6.25% (n=2)
Segmental resection (Reybard)	62	14.5%	8.06% (n=5)
Subtotal colectomy	8	1.9%	n=0

* Dehiscence of the rectal stump

Studying the correlation between leakage incidence and tumor features, we were able to find out that the feature which significantly influenced the occurrence of anastomotic leakage was stenosing, the occlusive one (p=0.003; OR=6.805; 95%CI: 1.54-29.99). Distant metastases (p=0.49) and the presence of carcinomatous ascites (p=1) did not increase the rate of occurrence of anastomotic fistulas.

A comparison of different kinds of variables regarding the patient, the operation and the tumor between the two groups of patients - with and without anastomotic fistula - is shown in table 3.

Discussions

The importance of anastomotic fistulas is given by the associated high mortality rate and a significant increase in the hospitalization duration and medical expenditure (Boccola et al 2011). In recent decades surgical techniques have developed, but the contribution of new surgical staplers, of laparoscopy and robotics did not determine the decrease of colorectal anastomotic fistulas, suggesting that physiopathological mechanisms leading to their occurrence are still unknown (Shogan et al 2013). The prevalence of anastomotic fistulas varies between 1% and 39%, the values ranging between very large limits due to the lack of standardized definitions of these complications. This aspect has been emphasized by Bruce (2001), who, analyzing 97 published studies, reported 56 definitions used to define fistulas after gastro-intestinal anastomoses. There are no

Table 3. Statistical significance of different kinds of variables

Variables		Group with fistula (n=18)	Group without fistula (n=409)	p
Type of surgery	**Emergency**	4 (4.49%)	85	0.775
	Elective	14 (4.14%)	324	
Surgical technique	**Laparoscopic**	0	22	0.613
	Classic	18 (4.44%)	387	
Type of anastomosis	**Manual**	13 (3.82%)	327	0.383
	With stapler	5 (5.7%)	87	
The surgical procedure	**Dixon**	5 (3.5%)	136	
	Hartmann I	1 (1.51%)	65	
	Right hemicolectomy	5 (4.23%)	113	
	Left hemicolectomy	2 (6.25)	30	
	Reybard	5 (8.06%)	57	
	Subtotal colectomy	0	8	
The tumoral factors	**Stenosis**	16 (6.75%)	221	0.003
	Without stenosis	2 (1.05%)	188	
	Metastasis	1 (1.6%)	60	0.49
	Without metastasis	17 (4.6%)	349	
	Ascites	1 (3.44%)	28	1
	Without ascites	17 (4.27%)	381	

controversies regarding the anastomotic leakage manifested by peritonitis clinical picture and the diagnosis is quite easy. It is not the same in leakages without obvious clinical signs and the diagnosis in those cases could be challenging. Even imaging studies cannot always highlight the fistula, even if it exists (Caulfield et al 2013).

The prevalence of fistulas in our study was 4.21% (18/427 patients). Values are similar to those published by Veyrie: 4% on 1750 patients operated for colorectal cancer (2007). Similar values were also reported by Walker et al (2004) who, on 1722 patients, reported 88 postoperative fistulas (5.1%), out of which 1.6% required emergency reoperation, and the remaining group of 3.5% was treated conservatively or by percutaneous drainage. Although there are studies which have shown that male gender is more prone to develop anastomotic leakage, the data obtained by us do not support this statement. The same findings were highlighted by Telem et al. (2010). Conversely, Walker et al (p=0.002) (2004) and McDermott (2015) found a significant correlation between male gender and leakage in a recent meta-analysis.

Age was another factor studied by us, and there have been no evidence of an association between this variable and the presence of fistulas (p=0.639). The lack of a correlation between age and fistulas has been reported by other authors as well (Walker et al 2004; Telem et al 2010; Trencheva et al 2013).

The type of surgery (emergency or elective) did not influence the occurrence of fistulas (p=0.775). The same findings were reported by Trencheva et al (2013), but a recent study (Sultan et al 2014) and a meta-analysis performed by McDermott (2015) reported that fistulas occur more frequently in emergency interventions (p=0.03).

Variables like approach type (open and laparoscopic) and the type of anastomoses (mechanical vs. manual) had no statistically

significantly influence on the leakage occurrence in our study. Telem et al (2010) and Trencheva (2013) found the same situation in their studies. The lack of a significant differences between fistulas and mechanical or manual anastomoses is explained by a prospective randomized study performed by Lustosa et al (2001) which, based on 1233 patients, demonstrated that the two techniques have similar results, both in terms of mortality and postoperative complications.

The highest incidence of fistulas was noticed after Reybard segmental resection. Colo-colic anastomosis seems to be at the highest risk of leakage 7/94 (7.44%), followed by ileocolic anastomosis 5/126 (3.9%) and colorectal anastomosis 5/141 (3.54%). An Italian study (Ruggiero et al 2011) reported a higher percentage of fistulas after colorectal anastomoses (16.6%) than colocolic (7.6%) or ileocolic (5.6%) anastomoses, the authors concluding that the location of anastomosis is the most important risk factor strictly linked to the anastomotic fistula rate. Regarding the colorectal anastomosis, other authors (Boccola et al 2011) had reported higher incidence of leakage rate than ours (3.5%) and we agree with authors who claim that the lower the anastomosis is performed the higher the incidence of leakage (Trencheva et al 2013).

Distant metastases and carcinomatous ascites did not statistically influence the leakage occurrence (p=0.49 respectively p=1). On the other hand, the stenosing, occlusive feature of the tumor was significantly associated with a higher rate of leakages compared to non-stenosing tumors (5.36% versus 1.13%) (p=0.003). There are studies in the literature which have examined the effect of co-morbidities on anastomotic fistulas. In a recent prospective study (Trencheva et al 2013) performed on 616 patients it was found that diabetes mellitus is not a significant factor. The results of the above mentioned study are consistent with ours, in which we found that diabetes is not a significant factor

that influences the development of fistulas (p=0.323). The incidence of insulin-dependent diabetes patients in the study group was 2.1% (9/427), only one of these patients developing anastomotic fistula.

Anemia, with hemoglobin below 10.5 g dl^{-1}, was another preoperative variable analyzed by us, being present in 156 of the studied patients. A percentage of 5.77% of these patients (n=9) developed fistula, but the value was not statistically significant. Contrary to these results, a study (Iancu et al 2008) reported that anemia with hemoglobin of 9.4g dl^{-1} is a predictive marker for anastomotic fistulas occurring after colorectal resections performed for neoplastic disease.

Conclusions

Our study revealed that Reybard segmental resections represent the highest risk of developing anastomotic leakage and the stenosing nature of the tumor is the most important predictor for fistula after surgery for colorectal cancer. These observations may lead to the recommendation to consider making a temporary or permanent diverting stoma in these patients. No anastomotic leakages were found in cases of laparoscopic approach, but we have to admit that the number of these operations is yet too low for a statistical purpose.

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