The Incidence and Mortality of Anastomotic Leakage after Colorectal Cancer Surgery

Gabriel Popescu¹, Daniela Sala², Miana Gliga¹, Sergiu Ciulic¹, Radu Mircu Neagoe¹,²* and Mircea Mureșan¹,²

¹Department of Surgery II, Emergency Mureș County Hospital, Târgu Mureș, Romania
²University of Medicine and Pharmacy of Târgu Mureș, Târgu Mureș, Romania

Abstract

Introduction: Anastomotic leakage (AL) remains one of the most feared complications after colorectal surgery with high mortality rates, prolonged hospitalization, highly risk of readmission, finally generating important costs for any healthcare system. AL prediction and early detection are a considerable challenge for each surgeon as no well-established and reliable predictors and diagnosis protocols are currently available.

Aims: To determine the incidence and mortality of AL after colorectal surgery, with identification of possible predictors and improvement points in the management of this complication.

Material and methods: We included 431 patients with colorectal cancer who underwent surgical resection and restoration of the digestive tube’s continuity, at the 2nd Department of Surgery, Emergency County Clinical Hospital of Târgu-Mureș, from January 2010-December 2015. The patients have been divided in two groups: AL group including 21 patients and no leak group with 410 patients. Demographic characteristics and comorbidities were recorded with clinical and laboratory follow-up in the postoperative period.

Results: There were no significant differences between the two groups in terms of demographic characteristics and comorbidities. The average age of patients with AL was 65.9 ± 11.6 vs. 65.0 ± 10.3 without AL. Male gender was predominant in both groups. No significant differences were recorded in terms of the localization and type of intervention between the two groups. Elevated C reactive protein levels were significantly more frequent in patients with AL (p=0.03). The mortality rate in patients with AL was significantly higher compared to the no leak group 28.6% vs. 1.9% (p<0.0001).

Conclusions: AL remains the most feared complication in colorectal surgery, with high mortality rates, regardless of the localization of the anastomosis and type of intervention. Elevated C reactive protein levels may predict AL being helpful for the early detection and treatment of this complication.

Keywords: Colorectal cancer; Colorectal resections; Anastomosis; Anastomotic leak; Postoperative morbidity; Postoperative mortality

Introduction

Colorectal cancer is one of the most commonly diagnosed cancers worldwide. Its incidence increases with age and higher mortality rate is encountered in men [1]. Therapeutic approach refers to a complex surgical, chemo-and radiotherapy treatment.

In spite of numerous surgical techniques developed in the last decades—including new mechanical stapler based methods—anastomotic leakage (AL) remains one of the most feared complications in colorectal surgery. Its incidence ranges from 1.5% to 16% for “per primam” anastomoses with frequent need for redo interventions, longer hospitalization and high mortality rates [2]. AL prediction and identification are still difficult due to its different clinical manifestations, varying from vague abdominal symptoms and prolonged postoperative ileus to fulminant abdominal pain in case of peritonitis and sepsis [3]. It is still a challenging task to distinguish early after surgery the developing septic process from the physiological inflammatory response; however, early diagnosis, before the appearance of clinical symptoms, remains essential for a long term survival [4]. The literature recognizes several risk factors for AL development such as diabetes, smoking, obesity, chronic kidney disease, cardiovascular diseases but facts are still contradictory [5-7]. According to several authors [8,9] characteristics of AL depend on many aspects:

- The direction of the leakage has a major impact on the patient’s symptoms; internal leakages are drained to organs such as the vagina, gallbladder or bladder and external leakages are drained through the teguments.

- AL’s may develop intra or extra peritoneal.

- Localizations of the AL may at the proximal or distal part of the anastomosis.

- The debit of the AL through the drain tube which could be small (<200 ml/24h), medium (200-500 ml/24h) or large (>500 ml/24 h).

- The severity of AL which might be minor (no clinical signs) or major (with clinical impact).

Numerous classifications are available, but no consensus exists over the medical world. The IMAGImE (International Multispecialty Anastomotic Leak Global Improvement Exchange) classification gives a simple clinical categorization of AL. Type A—with no or minimal clinical involvement, which does not need any active therapeutic intervention, Type B—which requires active treatment, but not surgical intervention and Type C—requiring surgical treatment [10].

*Corresponding author: Radu Mirecu Neagoe, University of Medicine and Pharmacy of Târgu Mureş, 2nd Department of Surgery, Emergency Mureș County Hospital, Târgu Mureș, Romania, Tel: +40 (0) 652 12 11 12 73; E-mail: neagorm@gmail.com

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This study aims to determine the incidence and mortality of AL after both elective and emergency procedures; we analyze possible AL’s predictors trying to identify improvement points in the management of this complication.

Material and Methods

In our study the clinical and operative charts (2nd Department of Surgery II, Emergency Mures County Hospital) were retrospectively analyzed between January 2010 and December 2015. We included 431 patients with colorectal cancer for whom surgical resection was performed with “per primam intentionem” restoration of the digestive tube’s continuity. The group of patients who developed AL was comparatively analyzed with those who did not exhibit this complication. Demographic characteristics and comorbidities of both groups were recorded; the type of surgical intervention, the localization and type of the anastomosis and the in-hospital mortality was determined for both groups. Patients with derivative surgical procedures were excluded, even if a later anastomosis was performed. No distinction was made between the types of procedures (manual or mechanical, continuous or separate sutures). Preoperative work-up included prophylactic antibiotic therapy, cardiology and pre-anesthesia examinations. The postoperative follow-up and diagnosis of AL was based on clinical signs (fever, ileus, abdominal pain, altered state of the patient), laboratory examinations (total blood count, urea, creatinine, procalcitonin, C reactive protein) and imaging studies (abdominal echography, abdominal computed tomography), according to local protocols. The study was approved by ethical commission of the institution and it was realized in accordance with ethical code of the Declaration of Helsinki.

Statistical Analysis

Statistical analysis was carried out using the SPSS for Windows (v 20.0, IBM Corporation, Armonk, NY, USA) software program. The Kolmogorov-Smirnov test was used to assess the normal distribution of continuous numerical variables. The results were presented as numbers and percentages for qualitative variables and as average ± standard deviation or median values for quantitative variables. Facts were compared using Student test (for quantitative variables) and χ² test (for qualitative variables) and a value of p<0.05 was considered statistically significant.

Results

Among 431 patients included 21 (4.9%) were identified with anastomotic leakage during hospitalization. All leakages were type C and needed surgical treatment. Primary emergency operation was performed for 1 patient (4.8%) from the group AL and for 33 patients C and needed surgical treatment. Primary emergency operation was performed for 1 patient (4.8%) from the group AL and for 33 patients C and needed surgical treatment. No significant difference was recorded, the type of surgical intervention, the localization and type of the anastomosis and the in-hospital mortality was determined for both groups. Patients with derivative surgical procedures were excluded, even if a later anastomosis was performed. No distinction was made between the types of procedures (manual or mechanical, continuous or separate sutures). Preoperative work-up included prophylactic antibiotic therapy, cardiology and pre-anesthesia examinations. The postoperative follow-up and diagnosis of AL was based on clinical signs (fever, ileus, abdominal pain, altered state of the patient), laboratory examinations (total blood count, urea, creatinine, procalcitonin, C reactive protein) and imaging studies (abdominal echography, abdominal computed tomography), according to local protocols. The study was approved by ethical commission of the institution and it was realized in accordance with ethical code of the Declaration of Helsinki.

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Results

Among 431 patients included 21 (4.9%) were identified with anastomotic leakage during hospitalization. All leakages were type C and needed surgical treatment. Primary emergency operation was performed for 1 patient (4.8%) from the group AL and for 33 patients (8%) in the group without AL (p=0.25). The average time to AL diagnosis was 6 days after the operation, with the earliest diagnosis on day 5th and the latest on day 13th. There was no significant difference between the two groups as regards demographic characteristics, associated comorbidities and risk factors such as diabetes, cardiovascular diseases, chronic kidney disease and obesity. The average age of patients with AL was 65.9 ± 11.6 vs. 65.0 ± 10.3 in the comparative group. Male gender was predominant in both groups, but with no significant difference between the two groups (Table I).

The majority of the tumors were localized at the level of the left colon (vascularized by the inferior mesenteric artery), with no significant difference between groups-42.8% in patients with AL vs. 38.8%, p=0.89. This location was followed by right colon tumors (vascularized by the superior mesenteric artery) with 28.6% (n=6) in the AL groups vs. 34.9% (n=6) in the no AL group. 28.6% of the AL cases were recorded (p=0.92). No left hemicolectomies and total colectomies were carried out in the anastomotic leak group. The type of anastomosis was identical in both groups, as proximal anastomoses (performed on the right colon) were more frequent than distal (performed on the left colon) ones (Table I).

The mortality rate was significantly higher in patients with AL compared to the no leak group (28.6% vs. 1.9%, p<0.0001). The average age of the deceased patients was 72 ± 12.52 years vs. 65 ± 10.37 years in the survivors of the AL group (p=0.11). There were no significant differences recorded in terms of the above-mentioned risk factors and comorbidities. Elevated C reactive protein levels (>5% over the accepted normal levels at the local laboratory) were significantly more frequently recorded in patients from the AL compared to the no leak group 85.71% (n=18) vs. 62.68% (n=257), (p=0.03).

Discussion

Anastomotic leaks still represent a major complication of colorectal surgery; however, no particular risk factors have been yet identified. It has been shown that male gender, smoking, obesity, and diabetes might represent risk factors for AL, due to the vulnerability of these patients; none of these were associated with higher incidence of AL in our study. Furthermore, the location of the tumor and anastomosis along with the type of intervention and surgical technique might also influence the development of AL [12]; in the current study no certain location or type of intervention proved to influence the AL’s appearance.

Usually AL is diagnosed between day 5th and 8th after the surgical intervention, those from first days being commonly associated with technical errors during surgery [13]. Early detection of this complication, thus avoiding a major peritonitis, is essential for the long-term survival of these patients [14]; in our study the average time of AL diagnosis was 6 days. Den Dulk at al. [15] proposed a clinical score for early detection of AL, so called “Dutch Leakage Score”, which analyzes different clinical and laboratory parameters. General vital signs such as fever (1 point), tachycardia (1 point), respiration frequency over 30/minute (1 point), diuresis-under 700ml/day or 30ml/hour (1 point), psychic-agitation or lethargy-and altered general state of the patient (1 point) along with local symptoms such as ileus, gastric stasis, evisceration or abdominal pain (2 points) are included. Laboratory parameters such as leukocytosis, elevated C reactive protein, creatinine, urea levels and parenteral feeding (1 point) are also part of the scoring system. The authors claimed that no diagnostic or therapeutic actions are needed ≤ 3 point; between 4-7 points severe monitoring is recommended and over 8 points contrast computed tomography is needed for diagnosis. This, yet not widely used score, might represent a useful tool in the early diagnosis of anastomotic leaks.

Anastomotic leaks detection, prior to the onset of clinical symptoms, is of paramount importance for better outcomes. In this study, no significant differences were observed as concerned the type of intervention; right hemicolectomy was most frequently performed in both groups (33.3% in the leak group vs. 36.4% in no leak group, p=0.94), followed by rectosigmoid resections (28.6% vs. 26.6%, p=0.95). Segmental colon resection of the colon was more often performed in the group with no leaks, but no significant difference was recorded (p=0.92). No left hemicolectomies and total colectomies were carried out in the anastomotic leak group. The type of anastomosis was identical in both groups, as proximal anastomoses (performed on the right colon) were more frequent than distal (performed on the left colon) ones (Table I).

Table I: Study population.

|                  | No leak n=410 (%) | Anastomotic leak n=21 (%) | P     |
|------------------|-------------------|---------------------------|-------|
| Age              | 65.0 ± 10.3       | 65.9 ± 11.6               | 0.69  |
| Male gender      | 210 (51.2%)       | 12 (57.4%)                | 0.59  |
| Diabetes mellitus| 113 (36.2%)       | 8 (38%)                   | 0.29  |
| Cardiovascular disease | 243 (59.2%) | 13 (61.9%)               | 0.81  |
| Chronic kidney disease | 97 (23.6%) | 5 (23.8%)                 | 0.98  |
| Obesity          | 281 (63.65%)      | 13 (61.9%)                | 0.87  |
perspective biomarkers could represent an objective indicator of the inflammatory process as a pathogenic substrate for AL development [16]. In a systematic review Su’a et al. [17] stated that systemic and peritoneal drainage fluid biomarkers cannot accurately predict the appearance of AL, but recommends the combination of these biomarkers for better results. In a recent study Smith et al. [18] defined the trajectory of C reactive protein as a possible gold standard biomarker for identification of anastomotic leaks after colorectal surgery. Our results also suggested that elevated C reactive proteins were significantly more frequently recorded in patients with AL than in the group without leakage.

The mortality rate after AL is high due to peritonitis with intense systemic inflammatory response and sepsis finally leading to multiple organ dysfunction or failure and death [19]. In our study, the mortality rate of patients with AL was highly significant in comparison with the survivors, but no significant differences were observed.

Conclusion

Anastomotic leaks still represent one of the major complications of colorectal surgery with high mortality rates regardless of the localization of the anastomosis or the type of intervention. Elevated C reactive protein levels might predict the appearance of this complication, thus facilitating an early diagnosis. Early detection and proper treatment remains a great challenge for every surgeon, because any delay in this process has a major impact on the survival of these patients with longer hospitalization and higher costs. Application of a score system which includes clinical, laboratory and imagistic parameters, along with detection of new risk factors should be useful for the reduction of the mortality of this feared complication.

Conflict of Interest

Authors have no conflict of interest to disclose.

References

1. Haggar FA, Boushey RP (2009) Colorectal cancer epidemiology: Incidence, mortality, survival, and risk factors. Clin Colon Rectal Surg 22: 191-197.
2. Hammond J, Lim S, Wan Y, Gao X, Patkar A (2014) The burden of gastrointestinal anastomotic leaks: an evaluation of clinical and economic outcomes. J Gastrointest Surg 18: 1165-1185.
3. Khan AA, Wheeler JM, Cunningham C, George B, Kettlewell M, et al. (2008) The management and outcome of anastomotic leaks in colorectal surgery. Colorectal Dis 10: 587-592.
4. Welsh T, von Frankenberq M, Schmidt J, Büchler MW (2011) Diagnosis and definition of anastomotic leakage from surgeon's perspective. Chirurg 82: 48-55.
5. Slim K, Joris J, Beloelil H (2016) Colonic anastomosis and nonsteroidal antiinflammatory drugs. J Visc Surg 153: 285-295.
6. Parthasarathy M, Greenamth M, Bowers D, Groot-Wassink T (2016) Risk factors for anastomotic leakage after colorectal resection: a retrospective analysis of 17518 patients. Colorectal Dis 19: 288-299.
7. Dekker JW, Liefers GJ, De Mol van Otterloo JC, Putter H, Tollenaa RA (2011) Predicting the risk of anastomotic leakage in left-sided colorectal surgery using a colon leakage score. J Surg Res 166: e27-34.
8. Wang S, Liu J, Wang S, Zhao H, Ge S, et al. (2017) Adverse effects of anastomotic leakage on local recurrence and survival after curative anterior resection for rectal cancer: A systematic review and meta-analysis. World J Surg 41: 277-284.
9. Shogam BD, An GC, Schardey HM, Matthews JB, Umanskiy K, et al. (2014) Proceedings of the First International Summit on Intestinal Anastomotic Leak, Chicago, Illinois, 2012. Surg Infct (Larchmt) 15: 479-489.
10. Rahbari N, Weitz J, Hohenberger W, Heald RJ, Moran B, et al. (2010) Definition and grading of anastomotic leakage following anterior resection of the rectum: A proposal by the International Study Group of Rectal Cancer. Surgery 147: 338-351.
11. Renuccozogullari A, Benice C, Valente M, Abbas MA, Renzi FH, et al. (2017) Predictors of anastomotic leak in elderly patients after colectomy: Nomogram-based assessment from the American College of Surgeons National Surgical Quality Program Procedure-Targeted Cohort. Dis Colon Rectum 60: 527-536.
12. Sliker JS, Daams F, Mulder IM, Jeekel J, Lange JF (2013) Systematic review of the technique of colorectal anastomosis. JAMA Surg 148: 190-201.
13. Feo LJ, Ijebi N, Ageirsson T, Dujovny N, Figg R, et al. (2014) Anastomotic leaks: Technique and timing of detection. Am J Surg 207: 371-374.
14. Daams F, Wu Z, Cakir H, Karsten TM, Lange JF (2014) Identification of anastomotic leakage after colorectal surgery using microdialysis of the peritoneal cavity. Tech Coloproctol 18: 65-71.
15. den Dulk M, Wiliviet MJ, Kortfam K, Neijenhuis PA, de Hingh IH, et al. (2013) The DULK (Dutch Leakage) and modified DULK score compared: actively seek the leak. Colorectal Dis 15: 528-533.
16. Fraccalvieri D, Biondo S, Saez J, Millan M, Kreisler E, et al. (2012) Management of colorectal anastomotic leakage: differences between salvage and anastomotic takedown. Am J Surg 204: 671-676.
17. Su’a BU, Mikaere HL, Rahiri JL, Bissett IB, Hill AG (2017) Systematic review of the role of biomarkers in diagnosing anastomotic leakage following colorectal surgery. Br J Surg 104: 503-512.
18. Smith SR, Pockney P, Holmes R, Doig F, Attia J, et al. (2017) Biomarkers and anastomotic leakage in colorectal surgery: C-reactive protein trajectory is the gold standard. ANZ J Surg.
19. Rickert A, Wiltieke F, Kienle P, Post S (2010) Management and outcome of anastomotic leakage after colonic surgery. Colorectal Dis 12: 216-223.