PREDICTIVE FACTORS OF POSTOPERATIVE SURGICAL COMPLICATIONS IN PATIENTS WITH EMERGENCY COLON CANCER SURGERY - A RETROSPECTIVE STUDY

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Abstract

Emergency colon cancer surgery is accompanied by high rates of postoperative complications. The study aims to identify factors that predict postoperative surgical complications in patients undergoing emergency surgery for colon cancer. We retrospectively analyzed the postoperative surgical complications on a group of 449 patients hospitalized and operated in an emergency for complicated colon cancer, in the General SurgeryClinics I and II of the County Emergency Clinical Hospital "St. Ap. Andrei "from Galați in the period 2008-2017. Patients' data were collected from medical notes, operation notes, imaging, and laboratory data, at the time of the emergency intervention. The predictive factors for the occurrence of postoperative surgical complications were: age<68 years, history of non-neoplastic pathology, Davies score 3 or 4, Charlson score> 3, and age-adjusted Charlson score > 10, presence of coagulation disorders, sepsis or acidosis at admission.

Keywords: complicated colon cancer, emergency surgery, postoperative surgical complications

Introduction

Data from the literature reveal that the morbidity of patients with emergency-operated colon cancers is higher than the morbidity of electively operated patients [1].
Depending on the time of onset, postoperative complications can be divided into early and late complications. Depending on their severity, they can be minor or major, and depending on the cause and treatment can be divided into surgical and non-surgical complications.

Postoperative surgical complications that occur after emergency treatment of colon cancer are anastomotic fistulas, intraperitoneal abscesses, peritonitis, postoperative intestinal occlusion, wound suppurations, intra-abdominal or parietal hematomas, evisceration, and complications of colostomy (necrosis, retraction, prolapse, stenosis).

The most common non-surgical postoperative complications are pulmonary complications (aspiration pneumonia, atelectasis, and pleural effusion), cardiovascular complications (thromboembolism, myocardial infarction, arrhythmias), and renal complications (renal failure) [2].

In perforated tumors, the wound infection is almost constant, taking into account the microbial load of stercoral peritonitis.

The most common major postoperative complications of segmental colectomies are hemorrhages or hematomas occurring following the slipping of vascular ligatures, anastomotic fistulas, abdominal abscesses, and ureter lesions in the case of sigmoid colectomies; and the minor ones - hematomas and parietal suppurations [3].

The major complication of colon resections, in addition to the complications common to any major surgery (hemorrhage, thromboembolism, evisceration, etc.) is the anastomotic fistula. The fistula has a multifactorial etiology being involved in endoluminal dysmicrobism or colic wall with ischemic distress (unprepared colon - occlusion), anastomosis performed in the septic environment (colic perforations), tared patient (elderly, anemic, cachectic, atherosclerotic), a non-puncture anastomosis, anastomosis in tension, septic shock in patients with colic perforations, etc.

Other studies show that the risk factors that increase the percentage of fistulas are old age, 1/3 straight tumors of the transverse colon, emergency surgery, mechanical suturing, LT anastomosis, and late resumption of intestinal motility [4, 5]. Diarrhea is due to the lack of the colon and the terminal ileum (place of fluid absorption) and the absence of the Bauhin valve (causes acceleration of transit)[6]. Injury to the spermatic or ovarian vessels leads to the appearance of a retroperitoneal hematoma [7].

The most common surgical complications of left hemicolectomy are anastomotic fistula, damage to the spleen, left ureter, mesenteric vessels, vena cava or aorta, poor hemostasis with hemorrhage or retroperitoneal hematoma [7].

The major risks of total and subtotal colectomies are the same as the risks of hemicolectomies: damage to the ureters, spleen, retroperitoneal hematoma, anastomotic fistula [7].

Complications of colostomies are generally surgical complications, but can also be minor complications being represented by prolapse, necrosis, retraction, or stenosis of the loop; ulcerations, hemorrhages, peristomal eventration [6].

The optimization of the management of the patient with emergency operated colon cancer implies the identification of the risk factors for the occurrence of postoperative surgical complications to correct those related to the medical-surgical act.

Material and method

From the group of 449 patients who presented as emergencies in the phase of colon cancer complications during 10 years, between 2008-2017, at the County Emergency Clinical Hospital "St. Apostol Andrei "from Galați and who benefited from surgical treatment in Clinics I and II GeneralSurgery, we selected a group of 106 patients who developed postoperative complications. The clinical notes, laboratory data, the operative protocols, and the anatomopathological reports were analyzed.

The clinical and epidemiological data taken into account were age, sex, personal history, general condition at admission, the presence of cachexia, and the duration from the onset of symptoms to presentation to a specialist.

The paraclinical data analyzed were the values of leukocytes, platelets, hemoglobin, hematocrit, glycemia, creatinine, proteins,

albumin, the presence of electrolyte disorders, acidosis, coagulation disorders, and the results of plain abdominal x-rays.

Intraoperative and treatment data include the location of the tumor, the presence of synchronous cancers, the time elapsed from hospitalization to surgery, the presence of local invasion or metastases, the type and duration of surgery, type of abdominal wall closure, antibiotics used, number of days of hospitalization.

Statistical correlations were made between the occurrence of postoperative surgical complications and epidemiological, clinical-paraclinical, intraoperative, and treatment data. The surgical complications were considered those that were due to the operative act.

Criteria for inclusion in the study: from the group of adult patients with malignant tumors of the colon (occlusion, perforation, hemorrhage) hospitalized in the General Surgery Clinics I and II of the Galati County Emergency Hospital during 2008-2017, patients with emergency operations that developed postoperative complications were enrolled.

Exclusion criteria from the study: patients who did not develop postoperative complications.

Study design

The patients included in the retrospective study were those with colon cancer, operated on in an emergency, who presented postoperative complications, for which epidemiological, clinical, paraclinical, and therapeutic factors were analyzed, to correlate them with the types of postoperative surgical / non-surgical complications.

Correlations of the type of complication occurred in the patients in the group with epidemiological data, personal history, hospitalization status, laboratory data, preoperative diagnosis, intraoperative diagnosis, type and duration of intervention, antibiotic regimen, and duration of hospitalization.

Statistical methods

Using SPSS version 23.0, statistical correlations were obtained, indicating the p-value with the Pearson Chi-Square and Likelihood Ratio tests for the nominal categorical variables. For continuous variables (Charlson, age-adjusted Charlson) we used ROC curves to identify a threshold value. Statistical conclusions were formulated using a significant difference threshold the value $p < 0.05$ for all calculations performed. To identify the predictive factors, the univariate logistic regression analysis was performed, specifying the relative estimated risk (OR), and it's 95.0% CI confidence interval. Multivariate logistic regression analysis was performed to determine a prediction model for postoperative surgical complications specifying for each predictor the estimated relative risk (OR) and its 95.0% CI confidence interval. Model accuracy was evaluated by the values of the Cox & Snell and Nagelkerke coefficients and the ROC curve area.

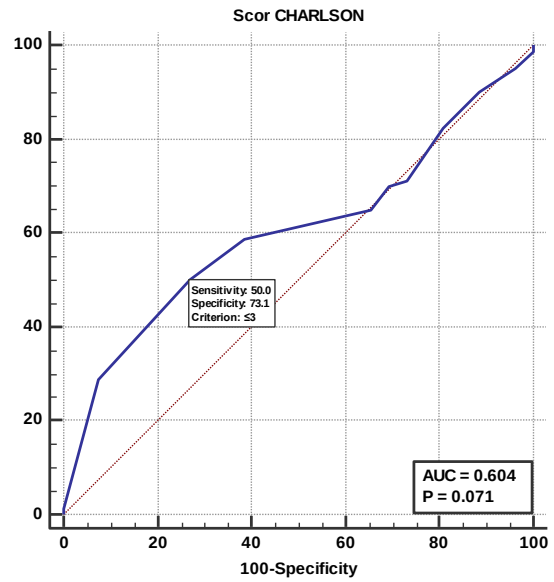
Results

Postoperative complications were also divided into surgical complications (75%) and non-surgical complications (25%). In the surgical complication group, we encountered wound infections, fistulas, bowel obstructions, abscesses, sepsis, and eviscerations. The non-surgical complications identified were heart failure, respiratory failure, acute renal failure, and Clostridium Difficile enterocolitis.

Approximately 5% of patients required re-operation. These interventions were, in order of frequency, reinterventions for adhesiolysis (38.09%), stoma formation (23.80%), evacuation of peritoneal abscesses (23.80%), resections followed by a new anastomosis (9.52%), and making a patch (4.76%).

Statistical analysis of postoperative surgical / non-surgical complications

To identify the threshold value of postoperative surgical complications for Charlson scores, we used ROC curves and the Youden index. (Fig.1, Fig.2)

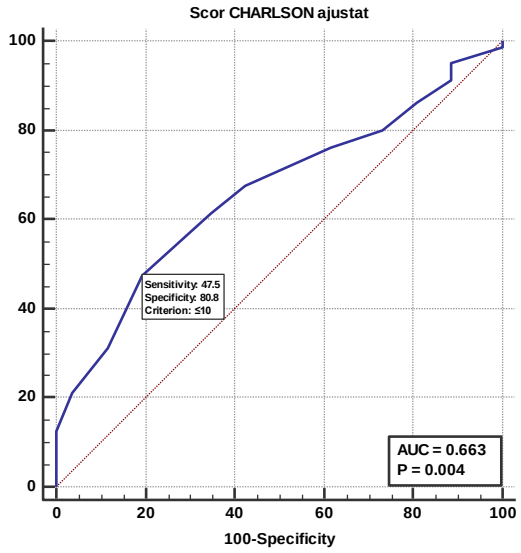


Youden index J	0.2308
Associated criterion	≤3
Sensitivity	50.00
Specificity	73.08

Figure 1 - Detection of the threshold value for the Charlson score that best discretizes patients with surgical complications

Statistical correlations and univariate regression analysis of postoperative surgical complications with epidemiological, clinical, laboratory, and treatment data are presented in Table 1.

Age ≤68 years was associated with the presence of postoperative surgical complications (p_value = 0.007343), the risk in these patients was O =5.11, 95%CI (1.41, 18.44) (p_value = 0.012735). Patients with a personal history of nonneoplastic pathology were associated with the presence of surgical postoperative complications (p_value= 0.028001), the risk in these patients was OR=0.20, 95%CI (0.04, 0.94) (p_value = 0.012735).



Youden index J	0.2827
Associated criterion	≤10
Sensitivity	47.50
Specificity	80.77

Figure 2 - Detection of the threshold value for the age-adjusted Charlson score that best discretizes patients with surgical complications

Patients with Davies score 1 were associated with the presence of surgical complications (p_value=0.044360), and regression analysis with reference to Davies score 1 indicates a difference from the other categories (p_value=0.005812). The risk in patients with a Davies score 3 was OR=0.11, 95% CI = (0.13,0.4) (p_value=0.000825), for those with a Davies score 4 was OR=0.06, 95%CI(0.00,0.76) (p_value=0.030176).

Patients with Charlson score>3 were associated with the presence of surgical complications, (p_value=0.039616), the risk in these patients was OR=0.36, 95%CI (0.14.0.97) (p_value=0.043871). Patients with age adjusted Charlson score >10 were associated with the presence of surgical complications, (p_value=0.010763), the risk in these patients was OR=0.26, 95%CI (0.09,0.76) (p_value=0.014422).

Patients with coagulation disorders at admission were associated with surgical

postoperative complications (p_value= 0.034364), the risk of surgical complications in these patients was OR=0.36, 95%CI (0.14, 0.94) (p_value=0.038039). Patients with sepsis at admission were associated with postoperative surgical complications (p_value=0.010100), the risk in these patients was OR=9.68, 95%CI (1.23, 075.84) (p_value=0.030603). Patients with the presence of acidosis at admission were associated with surgical postoperative complications (p_value=0.010967), the risk in these patients was OR=0.20, 95%CI (0.04, 0.94) (p_value=0.012735).

The duration of hospitalization<15 days was associated with the occurrence of postoperative non-surgical complications. (p_value=0.001048). The risk of surgical complications in patients with a hospital stay ≥15 days was OR = 7.77, 95%CI (1.79,12.70) (p_value=0.001756). (Table 1).

	Type=Chi	**TIP=nonChi**	**p_value**	**Logistic Regression**	
				p_value	**OR (95%CI)**
Age			**0.007343**([1])	**0.012735**	**5.11 (1.41, 18.44)**
>68 years(Ref)	48/80 (60%)	23/26 (88.5%)			
≤68 years	32/80 (40%)	3/26 (11.5%)			
SEX			0.534118 ([1])	0.534904	
F	30/80 (37.5%)	8/26 (30.8%)			
M	50/80 (62.5%)	18/26 (69.2%)			
app non neo =Yes	57/80 (71.3%)	24/26 (92.3%)	**0.028001**([1])	**0.012735**	**0.20 (0.04, 0.94)**
DAVIES Score			**0.044360** ([2])	**0.005812**([4])	
1 (Ref)					
2	36/80 (45.0%)	4/26 (15.4%)			
3	29/80 (36.3%)	7/26 (26.9%)		0.250131	
4	13/80 (16.3%)	13/26 (50.0%)		**0.000825**	
5	1/80 (1.3%)	2/26 (7.7%)		**0.030176**	**0.11 (0.03, 0.4)**
6	1/80 (1.3%)	0/26 (0.0%)		0.999623	**0.06 (0.00, 0.76)**
CHARLSON Score			**0.039616** ([1])	**0.043871**	**0.36 (0.14, 0.97)**
<=3 (Ref=0)	40/80 (50.0%)	7/26 (26.9%)			
>3	40/80 (50.0%)	19/26 (73.1%)			
Adj. CHARLSON Score			**0.010763** ([1])	**0.014422**	**0.26 (0.09, 0.76)**
<=10 (Ref=0)	38/80 (47.5%)	5/26 (19.2%)			
>10	42/80 (52.5%)	21/26 (80.8%)			
Coag disorders=Yes	17/80 (21.3%)	11/26 (42.3%)	**0.034364** ([1])	**0.038039**	**0.36 (0.14, 0.94)**
Sepsis=Yes	23/80 (28.8%)	1/25 (4.0%)	**0.010100** ([1])	**0.030603,**	**9.68 (1.23, 75.84)**
Acidosis=Yes	24/80 (30.0%)	15/26 (57.7%)	**0.010967** ([1])	**0.012735**	**0.20 (0.04, 0.94)**
X Ray			0.083289([2])	0.995033 ([4])	
0	9/80 (11.3%)	3/26 (11.5%)			
1	6/80 (7.5%)	2/26 (7.7%)			
2	54/80 (67.5%)	21/26 (80.8%)			
3	11/80 (13.8%)	0/26 (0.0%)			
LOC			0.809648 ([2])	0.832869 ([4])	
C18.0	10/80 (12.5%)	2/26 (7.7%)			
C18.2	4/80 (5%)	2/26 (7.7%)			
C18.3	7/80 (8.8%)	1/26 (3.8%)			
C18.4	11/80 (13.8%)	2/26 (7.7%)			
C18.5	7/80 (8.8%)	2/26 (7.7%)			
C18.6	7/80 (8.8%)	2/26 (7.7%)			
C18.7	26/80 (32.5%)	13/26 (50%)			
C19.0	8/80 (10%)	2/26 (7.7%)			
Preop diag			0.431334 ([2])	0.443113 ([4])	
H	1/80 (1.3%)	1/26 (3.8%)			
O	55/80 (68.8%)	20/26 (76.9%)			
P	24/80 (30%)	5/26 (19.2%)			
Surgery			0.509412 ([2])	0.496122 ([4])	
1	8/80 (10%)	5/26 (19.2%)			

	Type=Chi	TIP=nonChi	p_value	Logistic Regression	
				p_value	OR (95%CI)
2	32/80 (40%)	9/26 (34.6%)			
3	8/80 (10%)	4/26 (15.4%)			
4	32/80 (40%)	8/26 (30.8%)			
Op lenght			**0.047417** ([2])	0.478255 ([4])	
1 H (Ref)	5/80 (6.3%)	0/26 (0%)			
1,5 H	5/80 (6.3%)	5/26 (19.2%)			
2 H	24/80 (30%)	12/26 (46.2%)			
2,5 H	22/80 (27.5%)	3/26 (11.5%)			
3 H	20/80 (25%)	4/26 (15.4%)			
3,5 H	1/80 (1.3%)	1/26 (3.8%)			
4 H	2/80 (2.5%)	0/26 (0.0%)			
4,5 H	0/80 (0.0%)	1/26 (3.8%)			
5 H	1/80 (1.3%)	0/26 (0.0%)			
Antibiotics			**0.044360** ([2])	0.095470 ([4])	
1	37/80 (46.3%)	12/26 (46.2%)			
2	19/80 (23.8%)	12/26 (46.2%)			
3	11/80 (13.8%)	1/26 (3.8%)			
4	13/80 (16.3%)	1/26 (3.8%)			
Hospitalization			**0.001048** ([1])	**0.001756**	**7.77 (1.79, 12.70)**
<15 days(Ref)	29/80 (36.3%)	19/26 (73.1%)			
≥15 days	51/80 (63.8%)	7/26 (26.9%)			

1-Pearson Chi-Square, 2- Likelihood Ratio, 3-Fisher's Exact Test, 4- overall, Ref- reference
SEX F - female, M - male; app nonneo - nonneoplastic personal pathological history; Rx – plain abdominal X-ray, 0 - normal radiographs, 1 - diffuse excessive intestinal gas, 2 – air-fluid levels, 3 – pneumoperitoneum; LOC – localization - C18.0 - cecum, C18.2 - ascending, C18.3 - hepatic angle, C18.4 - transverse, C18.5 - splenic angle, C18.6 - descending, C18.7 - sigmoid, C19 - rectosigmoid junction; Preop diag- preoperative diagnosis, H - hemorrhage, O - occlusion, P – perforation; Surgery 1- colostomy, 2-tumor resection with a stoma, 3- internal derivation, 4- tumor resection with anastomosis; Antibiotics- 1 - third-generation cephalosporins, 2 - third-generation cephalosporins + metronidazole, 3 - Piperacillin + Tazobactam, 4 - carbapenems, Hospitalisation - number of hospital days, OR - the risk of occurrence of surgical postoperative complication)

Table 1 - Statistical correlations and univariate regression analysis of postoperative surgical complications with epidemiological, clinical, lab, and treatment data.

Multivariate logistic regression analysis

To obtain a model, in the multivariate regression were introduced all the significant or relatively significant variables obtained in univariate regression (age, history of non-neoplastic pathology, DAVIES score, Charlson score ≤3, age-adjusted Charlson score ≤10, coagulation disorders, septic condition, acidosis, type of antibiotic regimen, hospitalization days <15 days), the method used is stepwise.

Statistically significant remains only septic status (p_value = 0.0167), DAVIES score3 (p_value= 0.0031), DAVIES score 4 (p_value = 0.0052), antibiotic regimen type 2 (p_value = 0.0267), hospitalization ≥15 days (p_value= 0.0014) as predictors of postoperative surgical complications.

The risk of postoperative surgical complications in the group with sepsis was OR = 18.45, 95%CI [1.69, 200.0], in the group of patients with DAVIES 3 score is OR = 0.15, 95% CI [0.04, 0.53], in the group of patients with the DAVIES 4 score is OR = 0.01, 95% CI [0.001, 0.31], in the group with antibiotics scheme 2 is OR = 0.24, 95% CI [0.07, 0.85], in the group with hospitalization days ≥15 days is OR = 7.98, 95% CI [2.23, 28.50](Table 2)
This model explains in percentage of 31.43% (Cox & Snell R2) up to 47.16% (Nagelkerke R2) and the ROC curve reveals an area is 0.868 with 95% CI = [0.788, 0.926].

Variable	Odds ratio	95% CI
SEPSIS "yes"	18.45	1.69 to 200.0
Scor DAVIES=3	0.15	0.04 to 0.53
Scor DAVIES=4	0.01	0.001 to 0.31
Ab SCHEMA=2	0.24	0.07 to 0.85
Hospitalisation=" ≥15 Days"	7.98	2.23 to 28.50

Table 2 - Multivariate logistic regression analysis

Discussions

The morbidity identified in the study group was 24%. Postoperative complications were also divided according to operative act in surgical complications (75%) and non-surgical complications (25%). Postoperative complications were abscesses, sepsis, and evisceration. The non-surgical complications identified were heart failure, respiratory failure, acute renal failure, and Clostridium Difficile enterocolitis.

Age ≤68 years, sepsis at admission, and hospitalization<15 days were risk factors and history of nonneoplastic pathology, Davies score 3 or 4, Charlson score ≤3, age-adjusted Charlson score ≤10, coagulation disorders, acidosis at admission were protective factors. In our model, sepsis at admission and hospitalization ≥15 days were independent risk factors and DAVIES score 3 or 4 and the use of antibiotic regimen 2 (generation 3 Cephalosporins in combination with Metronidazole) were independent protection factors.

Unlike our results, in a comparative study of emergency and elective colon surgery, Smothers et al identified major postoperative complications at 44.82% for emergency surgery and 10.34% for elective cases. Regarding minor complications, these were 17.24% in emergency operated patients and 13.73% in electively operated patients. Overall morbidity was 64% for emergency operated patients and 24% for scheduled patients [8].

In a study on a large number of patients, Manceau et al. report for emergency colon surgery medical complications like-urinary tract infections (5%), heart complications (13%), lung complications (6%), thromboembolic complications (3%), and neurological complications (5%). Reported surgical complications were anastomotic fistulas (12%), parietal complications (12%), stoma complications (6%), hemorrhages (4%), prolonged postoperative ileus (5%), and unplanned reoperations (11%). Anastomotic fistulas occurred in 12% of patients [9].

In our study, anastomotic fistula occurred in 4.68% of patients. Biondo et al found that anastomotic fistula occurred in 15.8% of patients, being more common in patients with obstructions (17.4%) than in those with perforations (7.6%). 23.4% of patients had surgical wound infections, and 14.8% postoperative ileus. 17% of operated patients underwent surgical reoperations, unlike our results where only 5% of patients required surgical reinterventions.

In our study, there is no statistical significance between sexes and the occurrence of complications. In Biondo's study, it is shown that anastomotic fistula was more common in male patients. The author shows that 83.9% of fistulous complications occurred in patients with occlusions and 16.1% in those with perforations. We did not perform an analysis in this regard [10].

Recent data from the literature show that the risk of anastomotic fistulas in emergency patients is between 4 and 13% [11, 12]. Other studies show that the rate of anastomotic fistulas in right colon resections varies from 0.5 to 4.6% in an emergency, compared to 0.5-1.4% in cases of elective surgery. Regarding the left colon, the rate of fistulas is 3.5-30% in emergencies and only 5-10% in chronic cases [12, 13].

Beuran et al. report anastomotic cysts (on average 8.7% for emergency cases) in patients with occlusive tumors of the left colon were equal to those of patients operated electively (6.5%), less than in patients with hemorrhagic tumors (16%), being more common in stages III and IV, and the average age of patients with anastomotic fistula was 80 years. No statistically significant association was found between the presence of diabetes, pre-existing heart and vascular disease, and the appearance of fistulas. anastomotic. We have shown that Davies, Charlson, and age-adjusted Charlson comorbidity scores are predictors of postoperative surgical complications [1].

A study by Elod et al on a group of 236 patients in the period 2017-2018 and published in 2019 analyzed the safety of right hemicolectomy anastomoses performed for colon tumors. The results showed that the risk factors for anastomotic fistula are age, right 1/3 transverse colon tumors, and mechanical suture. While L-T anastomosis has been associated with most fistulas, L-L anastomosis is the safest. In our study, no statistical correlations were observed between the location of the tumor and the occurrence of surgical complications. We did not analyze the results of manual sutures compared to mechanical ones, nor did we follow the way of performing the anastomosis.

Conclusions

Risk factors for postoperative surgical complications were: age ≤68 years and sepsis at admission. History of non-neoplastic pathology, Davies score 3 or 4, Charlson score> 3 and age-adjusted Charlson score > 10, coagulation disorders or acidosis were protective factors for surgical postoperative complications.

The presence of sepsis at admission was an independent risk factor for surgical postoperative complications and the Davies score 3 or 4 and the use of antibiotic regimen 2 (Generation 3 cephalosporins in combination with Metronidazole) were independent protective factors.

Hospitalization longer than 15 days was associated with the presence of surgical postoperative complications.

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