

Surgery for Colorectal Cancer in Elderly Patients: How Could We Improve Early Outcomes ?

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ABSTRACT

Background: Age is one of the causes behind the undertreatment of elderly colorectal cancer patients. The increase of mortality among elderly colorectal cancer (CRC) patients is due to competing causes of death occurring in the early post operative period. The purpose of this study was to evaluate the risk factors for post operative mortality and morbidity among elderly CRC patients.

Materials and Methods: A retrospective descriptive chart review was performed on consecutive patients older than 70 y with CRC. We have collected data of 124 patients who were admitted from January 2001 to January 2010. Demographic characteristics, operative and postoperative informations were retrospectively analysed.

Results: Early postoperative morbidity, operation related to morbidity and mortality were observed in 44 (35.5%), 9 (7.3%) and 20 (16.1%) cases, respectively. No other factors but ASA

score ($p = 0.002$ and 0.005 in univariate and multivariate analyses, respectively) and emergency operations ($p < 0.001$ and 10^{-3} in univariate and multivariate analyses, respectively), were found to be risk factors of mortality. The results of multivariate analyses indicated that anaemia ($p = 0.021$) and rectal cancer ($p = 0.015$) had significant impact on the risk of anastomotic leakage. On the other hand, diabetes mellitus and rectal cancer were indicators that correlated with the width of hospitalization.

Conclusion: Elderly CRC patients should no longer be undertreated only because of their age. They should be exposed to more aggressive management than they are currently receiving. Careful preoperative evaluation, followed by medical optimization and planning of perioperative care could improve outcomes of colorectal surgery for elderly patients.

Keywords: Geriatric, Morbidity, Mortality

INTRODUCTION

Cancer is the second leading combined-sex cause of death among the 70-year-old and older age groups [1]. For this age and disease categories, colonic and rectal cancer forms the second leading combined-sex cause of mortality [2]. The geriatric CRC population is a very heterogeneous group, including patients with excellent health status and others with comorbid conditions, functional dependency, and limited life expectancy. Several studies found that elderly CRC patients who survive the first year have the same cancer-related survival as younger patients [3]. Therefore, the decreased survival among the elderly is mainly due to differences in early mortality. So, the treatment of elderly CRC patients should focus on perioperative care and the first postoperative month. Thus, the aim of the current study is to evaluate the single institution outcomes regarding the postoperative complication and mortality incidences, and analyse the risk factors that may be associated with these results.

MATERIALS AND METHODS

A retrospective descriptive chart review was performed on consecutive patients who are older than 70 y with CRC. We collected data from 124 patients who were admitted in our Department of Surgery (Hospital of Nabeul) starting from January 2001 to January 2010. Demographics characteristics, operative and postoperative information were retrospectively analysed. The aim of this study was to identify the incidences and risk factors for postoperative early morbidity and mortality after colorectal carcinoma surgery. Postoperative morbidity was categorized into two groups as surgical and non-surgical complications.

Since they were significant indicators for the success of the operation, factors that lengthen the hospitalization were also analysed. The following patients, disease or treatment related factors were

questioned in univariate and multivariate analyses: age, gender, severe anaemia (defined as 'present' if the patient required transfusion preoperatively), anaesthesia risk score (as defined by American Anesthesiology Association [ASA]), having a medical disease (diabetes mellitus, history of cardiac disease), stage and resection pattern.

The disease stage was determined according to the sixth edition of the TNM classification of the Union International Center of Cancer (UICC). The tumour classification of histomorphology follows the rules of the World Health Organization. All histopathological analyses were performed by a gastrointestinal histopathologist [4]. The tumour localization was classified into four groups: rectal cancers included tumours within a distance of 16 cm or less from the anal verge, measured with a rigid sigmoidoscope. All tumours above 16 cm from the anal verge were declared as colon cancers and subdivided in tumours of the sigmoid colon, left colon (including descending colon, left flexure and transverse colon) and right colon (including right flexure, ascending colon, cecum and appendix), according to the operation protocol. Colon resection was performed with a standardized regional lymph node dissection, and rectum resection with a total mesorectal excision, or partial mesorectal resection in upper third rectal carcinomas [4].

The study was approved by the Human Ethics Committee at the Mohamed Tahar Maamouri University Hospital of Nabeul, and it conformed to the provisions of the Declaration of Helsinki.

STATISTICAL ANALYSIS

Patient characteristics in both groups were compared using Chi-square with Fisher's exact test for qualitative variables. The normality of data was assessed by the the Shapiro-Wilk test and the Kolmogorov-Smirnov test. The Z Kolmogorov-Smirnov statistical

analysis was used for non-parametric continuous variables. Countable variables were defined with numbers and percentages.

Multivariate logistic regression model (Forward Stepwise method) was performed for identification of independent risk factors. α -value ≤ 0.05 was considered to be statistically significant.

The estimated probability "Pr" of the occurrence of complication or death is calculated according to the formula $Pr = 1/(1 + e^{-Z})$. In which, $Z = \beta_0 + \beta_1 X_1 + \dots + \beta_n X_n$ is a weighted sum of the values $X_1, \dots, X_n$ of risk factor, coded as 1 if present and 0 if absent, with $\beta_0, \dots, \beta_n$ as the weight or estimated regression coefficient. For each factor "f", the corresponding odds ratio "OR" is obtained from $OR_f = \exp(\beta_f)$. The baseline risk for a patient is estimated by $P = 1/(1 + e^{-\beta_0})$. The intercept " β_0 " means the baseline log odds of the event.

All analysis was carried with IBM SPSS 20 program for Windows.

RESULTS

A total of 124 consecutive patients were included in the study. 67% of all patients were referred to our department from the gastroenterology department and 33% were admitted from the emergency department. The median age was 75 years with extremes 70 to 96 years. Most of the patients were males 60.5% (n=75) with a sex ratio estimated as 3/2. The patients' characteristics and surgical data were shown in [Table/Fig-1].

Mortality risk factors [Table/Fig-2]: The incidence of mortality was 16.1% (n=20). The univariate analysis identified 7 dependent risk factors for postoperative death among elderly colorectal cancer

	Frequency (%)	Median [min-max]
Median Age		75 (70-96)
Gender		
Male	75 (60.5)	
Female	49 (39.5)	
ASA score		
I-II	64 (51.6)	
III-IV	60 (48.4)	
History of cardiac disease	19 (15.3)	
Diabetes mellitus	19 (15.3)	
Anemia at admission	21 (16.9)	
Type of surgery		
Palliative	28 (22.6)	
Curative	96 (77.4)	
Emergency admittance		
Emergent	42 (33)	
Not emergent	82 (67)	
Postoperative mortality	20 (16.1)	
Overall morbidity	9 (7.3)	
Specific morbidity	44 (35.5)	
Duration of hospitalization		12 days (1-54)

[Table/Fig-1]: Patient's characteristics

ASA: anesthesia risk score defined by American Anesthesiology Association

Total population (n=124)	Dead (n=20)	Alive (n=104)	P_u	$OR_u(95\% CI)$	P_m	β	$OR_m(CI\ 95\%)$
Age							
<85 years	13 (12%)	95 (88%)	0.005	5.7(1.8-17.9)	0.123		
≥ 85 years	7 (43.8%)	9 (56.2%)					
ASA score							
I-II	4 (6.2%)	60 (93.8%)	0.002	5.45(1.7-17.45)	0.005	1.793	6(1.725-20.93)
III-IV	16 (26.7%)	44 (73.3%)					
Diabetes mellitus							
Yes	5 (26.3%)	14 (73.7%)	0.19				
No	15 (14.3%)	90 (85.7%)					
Anemia							
Yes	3 (14.3%)	18 (85.7%)	0.8				
No	17 (16.5%)	86 (83.5%)					
Cardiac disease							
Yes	6 (31.6%)	13 (68.4%)	0.047	3(0.98-9.186)	0.31		
No	14 (13.3%)	91 (86.7%)					
Emergency admittance							
Yes	15 (35.7%)	27 (64.3%)	$<10^{-3}$	8.56(2.83-25.78)	0.94		
No	5 (6.1%)	77 (93.9%)					
Obstruction							
Yes	13 (37.1%)	22 (62.9%)	$<10^{-3}$	6.9(2.46-19.43)	0.9		
No	7 (7.9%)	82 (92.1%)					
Bowel perforation							
Yes	5 (50%)	5 (50%)	0.01	6.6(1.7-25.54)	0.22		
No	15 (13.2%)	99 (86.8%)					
Resection class							
R0	13 (12.4%)	92 (87.6%)	0.015	4.13(1.37-12.38)	0.34		
R1	7 (36.8%)	12 (63.2%)					
Rectum							
Yes	7 (14.9%)	40 (85.1%)	0.7				
No	13 (16.9%)	64 (83.1%)					
Emergency surgery							
Yes	15 (36.6%)	26 (63.4%)	$<10^{-3}$	9(2.98-27.18)	$<10^{-3}$	2.27	9.7(3.03-30.98)
No	5 (6%)	78 (94%)					

[Table/Fig-2]: Univariate and multivariate analysis: mortality risk factors in elderly colorectal cancer patients

ASA: anesthesia risk score defined by American Anesthesiology Association; P_u : univariate p-value; P_m : multivariate logistic regression P value; OR_u : univariate odds Ratio; $OR_m(CI\ 95\%)$: multivariate logistic regression Odds Ratio; CI: confidential Interval. β_{0u} : -3.903

patients: the age ≥ 85 y ($p=0.005$), the ASA III-IV score ($p=0.002$), the history of cardiac disease ($p=0.047$), the emergency admittance ($p<10^{-3}$), the bowel obstruction ($p<10^{-3}$), the bowel perforation ($p=0.01$), the palliative surgery ($p=0.015$) and the emergency surgery $<10^{-3}$.

The logistic regression analysis confirmed the ASA III-IV score ($p=0.005$; OR=6; confidential Interval (CI)95%: 1.725-20.93) and the emergency surgery ($p<10^{-3}$; OR: 9.7 CI95%: 3-31) as independent predictive factors for postoperative death. Based on these results, we developed a predictive model to calculate the probability (Pr) of the risk of postoperative death: $Pr=1/(1+e^{-Z})$; where $Z=-3.903+1.7$ (ASA III-IV Score {yes=1;No=0}) + 2.2 (emergency surgery {yes=1;No=0}).

The baseline risk was estimated as 1.97%. If the patient had both independent factors, the probability of death will be 50%.

Risk factors for specific complications [Table/Fig-3]: The univariate analysis showed that the anaemia ($p=0.044$), the diabetes mellitus ($p=0.031$) and patients operated for rectal cancer ($p=0.026$) increased the risk to develop a specific complication. The multivariate analysis confirmed that anaemia ($p=0.021$; OR=6.1; CI95%: 1.32-28.3) and patients operated for rectal cancer ($p=0.015$; OR=8.07; CI95%: 1.49-43.8) were the two independent risk factors for specific complications.

Risk factors for non-specific complications [Table/Fig-4]: The emergency admittance ($p=0.026$), the bowel obstruction ($p=0.006$) and the emergency surgery ($p=0.046$) were identified as dependent risk factors for non-specific complications in the postoperative period. In the multivariate analysis, only the bowel obstruction was considered as an independent risk factor ($p=0.008$; OR=3.29; CI95%: 1.37-7.89).

Hospitalization period [Table/Fig-5]: The duration of hospitalization was lengthened for patients with diabetes (19 Vs 12 days; $p=0.016$) and patients operated for rectal cancer (15 Vs 11.5 days; $p=0.048$).

DISCUSSION

Colorectal cancer (CRC) is an elderly disease. The mean age at diagnosis is 72 y, with 70% of cases occurring among patients aged 65 y and 40% of cases among patients aged 75 y [5,6]. Based on the aging demographics [4,7], we can expect that the number of elderly CRC patients might increase in the coming years. The geriatric CRC population is a very heterogeneous group, including patients with excellent health status and others with comorbid conditions, functional dependency, and limited life expectancy [8]. These issues could account for the fact that a significant proportion of elderly CRC patients is undertreated in comparison with younger patients [9-11]. Clinicians frequently have to decide whether major surgery is justified in elderly patients with a limited life expectancy. Effectiveness of surgery in elderly patients depends on whether it is done safely, allowing patients to return to productive lives, with a postoperative life expectancy that is improved by the surgical procedure [11]. Although improvements in surgical techniques, anaesthetic procedures, and postoperative care have all made surgery less hazardous, few elderly patients undergo resection for colorectal cancer in comparison with their younger counterparts [12].

Notwithstanding all these differences, several studies found similar disease-specific survival for elderly and young colorectal cancer patients [13,14]. This would indicate that the increase of mortality in elderly colorectal cancer patients is due to competing causes of

Total population (n=124)	Yes (n=9)	No (n=115)	P_u	OR _u (95% CI)	P_m	β	OR _m (CI 95%)
Age							
<85 years	7 (6.5%)	101 (93.5%)	0.38				
>85 years	2 (12.5%)	14 (87.5%)					
Rectum							
Yes	7 (14.9%)	40 (85.1%)	0.026	6.56 (1.3 – 33)	0.015	2.089	8.07(1.49-43.8)
No	2 (2.6%)	75 (97.4%)					
Anemia							
Yes	4 (19%)	17 (81%)	0.044	4.6 (1.12-18.92)	0.021	1.809	6.1(1.32-28.3)
No	5 (4.9%)	98 (95.1%)					
Diabetes mellitus							
Yes	4 (21.1%)	15 (78.9%)	0.031	5.3 (1.28-22.11)	0.059		
No	5 (4.8%)	100 (95.2%)					
Obstruction							
Yes	2 (5.7%)	33 (94.3%)	0.67				
No	7 (7.9%)	82 (92.1%)					
Resection class							
R0	7 (6.7%)	98 (93.3%)	0.55				
R1	2 (10.5%)	17 (89.5%)					
Bowel perforation							
Yes	0 (0%)	10 (100%)	0.36				
No	9 (7.9%)	105 (92.1%)					
Emergency admittance							
Yes	2 (4.8%)	40 (94.3%)	0.44				
No	7 (8.5%)	75 (91.5%)					
Cardiac disease							
Yes	2 (10.5%)	17 (89.5%)	0.55				
No	7 (6.7%)	98 (93.3%)					
Emergency surgery							
Yes	2 (4.9%)	39 (95.1%)	0.47				
No	7 (8.4%)	76 (91.6%)					

[Table/Fig-3]: Univariate and multivariate analyses: Risk factors of specific complications in elderly colorectal cancer patients.

ASA: anesthesia risk score defined by American Anesthesiology Association; P_u : univariate p-value; P_m : multivariate logistic regression p-value; OR_u: univariate odds Ratio; OR_m(CI 95%): multivariate logistic regression Odds Ratio; CI: confidential Interval. β : 4.254

Total population (n=124)	Yes (n=29)	No (n=95)	P _u	OR _u (95% CI)	P _M	β	OR _M (CI 95%)
Age							
<85 years	26 (24.1%)	82 (75.9%)	0.76				
≥85 years	3 (18.8%)	13 (81.2%)					
ASA							
I -II	18 (28.1%)	46 (71.9%)	0.19				
>II	11 (19.3%)	49 (81.7%)					
Diabetes mellitus							
Yes	8 (42.1%)	11 (57.9%)	0.07				
No	21 (20%)	84 (80%)					
Anemia							
Yes	4 (19%)	17 (81%)	0.6				
No	25 (24.3%)	78 (75.7%)					
Cardiac disease							
Yes	8 (42.1%)	11 (57.9%)	0.07	2.9 (1.04-8.13)	0.68		
No	21 (20%)	84 (80%)		2.9 (1.04-8.13)	0.11		
Emergency admittance							
Yes	15 (35.7%)	27 (64.3%)	0.026	2.7 (1.14-6.33)	0.85		
No	14 (17.1%)	68 (82.9%)					
Obstruction							
Yes	14 (40%)	21 (60%)	0.006	3.29 (1.37–7.89)	0.008	1.191	3.29(1.37-7.89)
No	15 (16.9%)	74 (83.1%)					
Emergency surgery							
Yes	14 (34.1%)	27 (65.9%)	0.047	2.35 (1-5.52)	0.46		
No	15 (18.1%)	68 (81.9%)					
Bowel perforation							
Yes	2 (20%)	8 (80%)	0.79				
No	27 (23.7)	87 (76.3%)					
Resection class							
R0	23 (21.9%)	82 (78.1%)	0.36				
R1	6 (31.6%)	13 (68.4%)					

[Table/Fig-4]: Univariate and multivariate analyses: risk factors of non-specific complications in elderly colorectal cancer patients. Abbreviations: ASA: anesthesia risk score defined by American Anesthesiology Association; P_u: univariate P value; P_M: multivariate logistic regression P value; OR_u: univariate odds Ratio; OR_M(CI 95%): multivariate logistic regression Odds Ratio; CI: confidential Interval. β₀ = -1.596

death [3]. When survival data for CRC are corrected for expected death from other causes and first-month mortality, age differences disappear [3]. Therefore, decreased survival in the elderly is mainly due to differences in early mortality. These studies imply that, in treating elderly colorectal cancer patients stage I–III, the focus should be on the perioperative process and the first postoperative Month [3].

In the current study, ASA score and emergency operations were the only independent risk factors for perioperative death, in multivariate analysis. On the other hand, age ≥ 85 y, cardiovascular morbidity, intestinal obstruction and palliative surgery, were associated with significantly higher perioperative mortality rate. However, in the multivariate analysis, all these effects disappeared. We think that these results are interesting. In fact, a series of scoring systems were used to define the preoperative morbidity and mortality risks of colorectal carcinoma. The most frequently used scoring system is ASA score which has been developed by anesthesiologists and actually defines the risks of anaesthesia. It has been proved, in the current study, that ASA score is really a good indicator to estimate postoperative mortality in colorectal carcinomas among the elderly. Thus, careful patient selection with preoperative evaluation, mainly for ASA III-IV patients, is of great importance. On the other hand, we think that every effort should be set in place to avoid urgent operations and the use of intraluminal stents should be divulged as a bridge-to-surgery in order to allow full compensation of anaemia, malnourishment, hydro-electrolytic derangement and depression [15,16]. As the highest operative mortality rates are recorded for older individuals undergoing emergency surgery, the participation of this age group into screening programs might decrease the

prevalence of the acute presentation.

In the present study, univariate analyses (log-rank test) showed that the following factors were associated with specific complications (anastomotic leakage): severe anaemia, diabetes mellitus and rectal cancer. The results of multivariate analyses indicated that only anaemia and rectal cancer had significant impact on the risk of anastomotic leakage. These results imply that more attention should be given to patient selection and careful preoperative evaluation, followed by medical optimization, proper timing of surgery, and planning of perioperative care. On the other hand, we think that the use of loop ileostomy or loop transverse colostomy represents an important issue for temporary decompression of colorectal anastomosis, in rectal cancer, since it was an independent risk factors for anastomotic leakage, in multivariate analysis.

The current study also questioned the factors which lengthen the hospitalization period, and revealed that diabetes mellitus and rectal cancer were indicators that correlated with the width of hospitalization. We think that this factor is very important for elderly patients because it has been proved that increased length of hospitalization was significantly associated with functional decline at the time of discharge (delirium, undernutrition, functional impairment, depression) [17,18].

LIMITATIONS

The current study may be criticized for including some limitations, mostly related to its retrospective design and the data of a single institution. But, as most recent studies aimed at comparing population-based survival data for young and elderly, and as it has been proved that elderly patients have a higher rate of comorbidity

	Hospitalization Median (min-max)	p
Age		
<85 years	14 (2-54)	0.91
≥85 years	12 (6-45)	
Emergency surgery		
Yes	12 (6-45)	0.067
No	14.5 (5-54)	
Rectum		
Yes	15 (2-54)	0.048
No	11.5 (5-46)	
Emergency admittance		
Yes	10 (2-45)	0.11
No	14 (5-54)	
Diabetes mellitus		
Yes	19 (5-54)	0.016
No	12 (2-46)	
Obstruction		
Yes	10 (5-45)	0.21
No	14 (2-54)	
Cardiac disease		
Yes	13 (2-46)	0.91
No	13 (2-46)	
Anemia		
Yes	18 (6-45)	0.11
No	12 (2-54)	

[Table/Fig-5]: Comparison of the risk factors which can affect the duration of hospitalization

and a higher postoperative 30-day mortality rate, we choose to focus on this critical period in the management of elderly colorectal cancer.

CONCLUSION

Because of improvements in surgical techniques, anaesthetic procedures, and postoperative care, elderly patients should be exposed to more aggressive management than they are currently receiving. Aggressiveness of management of any disease should be decided solely by the ability to withstand that management which is always assessed by functional status. The treatment should be intensive, appropriate, safe, effective and should be adjusted to take account of the biological age and comorbidities in order to maximize survival. In today's time, for a disease like CRC when the treatment is usually planned, the patient can be shifted to a well endowed facility. In the current study, ASA score and emergency operations were the only independent risk factors for peri-operative

death, in multivariate analysis. On the other hand, anaemia and rectal cancer had significant impact on the risk of anastomotic leakage. It is for this reasons that every effort should be set in place to avoid urgent operations. Besides, careful preoperative evaluation, followed by medical optimization and planning of perioperative care could improve outcomes of colorectal surgery for elderly patients. No conflict of interest

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