

# Clinico-Pathological Characteristics, Therapeutic Features and Post-operative Course of Colorectal Cancer in Elderly Patients

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## ABSTRACT

**Statement of Problem:** Colorectal cancer is predominantly a disease of elderly people and is a major cause of morbidity and mortality in the elderly population. The geriatric colorectal population is a very heterogeneous group, including patients with excellent health status and others with comorbid conditions, functional dependency, and limited life expectancy.

On the other hand, the effectiveness of surgery for colorectal cancer depends on it being carried out safely, which allows most patients to return to productive lives, with an improved post-operative life expectancy or at least one that is not diminished by the surgery.

**Materials and Methods:** This work is a descriptive study of a retrospective cohort, based on administrative databases, of all patients with colorectal cancer diagnosed or treated in our institution. We extracted data on sociodemographic

characteristics, comorbidity, type of cancer, stage of cancer, type of treatment received, post-operative complications and cause of post-operative death. We compared differences between an elderly group (Group A) (age >75 years) and a group of patients below 75 years (Group B).

**Results:** We found that elderly patients with colorectal cancer were more likely to be operated in emergent conditions, had more non-specific complications and more post-operative mortality than patients below 75 years. On the other hand, tumours stages, tumours characteristics and post-operative specific morbidity have been proved to be similar, both in Group A and Group B patients.

**Conclusion:** These results suggest that surgery is feasible and can be safe for patients above 75 years, but it needs much more evaluation of comorbidities, pre- and post-operative intensive care to avoid post-operative non-specific complications.

**Keywords:** Colorectal cancer, Colectomy, Post-operative mortality, Post-operative morbidity

## INTRODUCTION

Colorectal cancer is a major cause of morbidity and mortality in the elderly population. The number of cases in elderly people is expected to increase as the population ages. Various population based studies show that survival of elderly colorectal cancer patients is worse compared with younger patients.

Differences in survival by age-group in colorectal cancer may be explained by variations in tumour factors, patient characteristics, and therapy. Colorectal cancer is managed with surgical resection of the primary tumour whenever possible, either for cure or palliation, to avoid late complications, such as obstruction and perforation. The surgical procedure chosen depends mainly on the position of the tumour in the bowel and whether the patient presents electively or as an emergency. Clinicians frequently have to decide whether major surgery is justified in elderly patients with a limited life expectancy.

We compared in this study clinical and histopathologic characteristics of colorectal cancer in patients below and above 75 years; we analyzed the post-operative course and morbi-mortality in these patients.

## MATERIAL AND METHODS

The records of 280 patients with colorectal cancer, who were admitted between 2001 and 2010 in the Department of Surgery, Hospital of Nabeul (north east of Tunisia), were retrospectively analysed. The age of 75 was used to separate the patients into two groups: patients above 75 years (Group A) and patients below 75 years (Group B). Of these patients, 56 (20%) were older than 75 years.

74.6% of all patients were referred to our department from the Gastroenterology department and 25.4% were admitted from the Emergency department.

The clinical data of each of these patients were analysed for age at time of operation, sex, performance status, location of tumour, stage, tumour differentiation. Disease stage was determined according to the sixth edition of the TNM classification of the Union Internationale Contre le Cancer (UICC). Tumour classification of histomorphology follows the rules of the World Health Organization. All histopathological analysis were performed by a gastrointestinal histopathologist.

The tumour localisation was classified in 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

Histopathologic characteristics	Group A	Group B	p
Undifferentiated	8.9%	15.6%	0.071
Vascular Invasion	44%	51%	0.22
Perinervous Invasion	28%	34%	0.27
R0 Resection	87.5%	86.6%	0.5
T3-4	76%	85%	0.1
N+	60%	67%	0.23

**[Table/Fig-1]:** Histopathologic characteristics of colorectal cancer in old patients (Group A) vs. young patients (Group B)

	Group A	Group B	p
Nonspecific complications	25%	12%	0.016
Specific complications	12.5%	12.05%	0.5
Second interventions	16%	10%	0.18
Post-operative mortality	21%	4.4%	0.0001

**[Table/Fig-2]:** Post-operative course of elderly colorectal patients (Group A) vs. young colorectal patients (Group B)

(including right flexure, ascending colon, cecum and appendix), according to the operation protocol. Colon resection was performed with a standardised regional lymph node dissection and rectum resection with a total mesorectal excision or partial mesorectal resection in upper third rectal carcinomas.

All statistical analysis were evaluated using the statistical software Statistical Package for Social Sciences (SPSS) for Windows (version 17.0, SPSS Inc., Chicago, IL, USA). Variables were compared by the chi-square test.

Patient characteristics were compared using chi-square with Fisher's exact test for qualitative variables and using the Student t-test for quantitative variables.  $p$ -value  $\leq 0.05$  was considered to be statistically significant. The discriminating value for the continuous dependent factors was investigated by calculating the area under a Receiver Operating Characteristics (ROC) curve.

## RESULTS

Out of the total 280 patients that have been operated for colorectal cancer, between 2001 and 2010, 56 were older than 75 years (20%). 51.7% of these patients were male and 48.3% were female. There were no significant differences in sex distribution between the group of patients above 75 years (Group A) and the group of patients below 75 years (Group B):  $p=0.24$ .

The median age of all patients with colorectal cancer was 59.2 years (range 14-96). In Group A, the median age was 78 years (range 75-96) and among Group B it was 54 years (range 14-73).

Emergency operations were more common among patients over 75 years of age than those below 75 years: 35.7% vs. 22.3% respectively, ( $p=0.017$ ). Indications for emergency surgeries were stenoses ( $n=18$ ) and perforations ( $n=6$ ).

Among Group A patients, 35 underwent elective surgery. All symptoms declared at admission to the hospital, except abdominal pain which was more frequent in Group B patients (51% in patients  $\leq 75$  years vs. 39.5% in patients  $>75$  years;  $p=0.03$ ), showed an equal distribution in patients under and over 75 years of age. The most frequent presenting complaints for Group A patients were per-anal bleeding (35%), weakness (25%), constipation (18%), a recent change in bowel habits (14.2%) and paradoxical diarrhea (9%). In most, symptoms were multiple; all these patients underwent colonoscopy and biopsies.

In Group A patients, 34% of the tumours were located in the right colon (vs. 20% of Group B patients;  $p=0.024$ ), 34% in the left colon, and 32% in the rectum.

Group A patients showed significant differences within the American Society of Anesthesiologists (ASA) classification I-III (higher ASA classifications,  $p=0.0001$ ).

At laparotomy, there were hepatic metastasis in 12.5% of cases (vs. 14.7% of cases in Group B patients,  $p=0.8$ ), and peritoneal metastasis in 9% of cases (vs. 10.7% of cases in Group B patients,  $p=0.76$ ). The operation was curative in 90% of the cases and palliative in 10% of the cases. A right colectomy was done in 28.5% of cases, a left colectomy in 9% of the cases, a sigmoidectomy in 14.2% of the cases, a total colectomy in 10.7% of the cases, an anterior rectal resection in 25% of cases, an abdomino perineal resection in 1.8% of cases and a colostomy in 10.7% of the cases.

Histological study of resected specimens did not show significant differences between Group A and Group B patients, concerning

tumours stage, lymphatic invasion, venous invasion, perineural invasion and tumours differentiation [Table/Fig-1].

87.5% of Group A patients had R0 resection vs. 86.6% of Group B patients ( $p=0.5$ ).

Post-operative nonspecific morbidity was significantly higher in older patients (25% for Group A patients vs. 12% for Group B patients  $p=0.016$ ). On the other hand, there were no significant differences, between the two groups, concerning specific complications, such as anastomotic leakage (12.5% for Group A vs. 12.05% for Group B  $p=0.5$ ) and no differences in second intervention rate ( $p=0.18$ ). Nevertheless, post-operative mortality was significantly higher in Group A (21% vs. 4.4%  $p=0.0001$ ) [Table/Fig-2].

There were no significant differences between the two groups concerning post-operative stay in hospital: median length of stay was 15.14 days for Group A patients vs. 16.4 days for Group B patients.

In Group A, only one patient, having a rectal cancer, received pre-operative radiotherapy. Group B patients were more likely to receive pre-operative radiotherapy or radio chemotherapy:  $p=0.028$ .

On the other hand, three patients in Group A received post-operative chemotherapy for advanced colic cancer. Group B patients were more likely to receive post-operative chemotherapy:  $p=0.0001$ .

Median follow-up for Group A patients was 14 months. In the first year, only one patient died (hepatic and peritoneal metastasis). Two patients were admitted for non-specific complications: intestinal obstruction.

## DISCUSSION

Cancer is the second leading combined-sex cause of death in the 75 years and older age-group. In this age and disease category, colonic and rectal cancer forms the second leading combined-sex cause of mortality [1]. The number of old people in our society is increasing and so is the number of elderly people with colorectal cancer [2].

The exact reasons are unknown, but theories of cancer development in the elderly are applicable to colorectal cancer: (1) longer duration of exposure and increased cellular susceptibility to carcinogens, (2) diminished ability to repair damaged DNA, (3) oncogene activation or amplification and tumour suppressor gene loss or malfunction, and (4) diminished immune surveillance mechanisms [3,4].

As shown in previous publications, the median age of Tunisian patients with colorectal cancer, was younger than the age described in most developed countries [5].

We showed in the present study, an equal distribution of symptoms, in patients under and over 75 years of age. The most frequent symptoms were per-anal bleeding (35%), weakness (25%), constipation (18%), a recent change in bowel habits (14.2%) and paradoxical diarrhea (9%). Only abdominal pain was more frequent in patients below 75 years ( $p=0.03$ ). Early recognition of colorectal cancer in patients over age 75 requires clinical awareness and aggressive pursuit of symptoms. On the other hand, colorectal cancers in old patients are more likely revealed by a complication, this fact is related to delay in diagnosis in old patients and this is due to negligence of symptoms in these patients [6].

We can say that awareness of the risk of colorectal cancer in elderly patients is required to prevent late presentation and the more frequent need for emergency surgery in this age-group.

Unlike another recent study which was unable to find differences between patients below 75 years and patients above 75 years in tumour location [7], we found that the tumours were located much more in the right colon for patients over 75, for the other locations there were no significant differences for both groups.

Surgery is the treatment of choice for stages I-III of the disease and several subsets of stage IV colon cancer [8]. Despite advances

in surgical techniques and post-operative care that make surgery safer in the elderly, age continues to affect treatment choice and curative cancer-directed surgery is less frequent in older patients. [6,9]. However, several studies show that surgery is feasible to treat colorectal cancer in elderly patients [10,11] even in octogenarians [12]. For our patients, there were no significant differences concerning curative or palliative surgery ( $p=0.38$ ).

Specimen's analysis did not show significant differences between patients over and under the age of 75, concerning tumours stage, lymphatic invasion, venous invasion, perineural invasion and tumours differentiation. We think that this fact is important because all these parameters are independent factors in cancer-specific survival [6].

Published results for tumours pathological characteristics are conflicting: some studies show more advanced stages in old patients [6] whereas others do not [13].

According to previous studies, we found that the frequency of post-operative morbidity and mortality seemed to increase progressively with advancing age, but the interpretation of these findings is limited by the absence of clear and consistent definitions of these outcomes [6]. An increasing frequency of respiratory and cardiovascular complications, stroke, and thromboembolism was reported in relation to age [14], although anastomotic leakage rates were unchanged. This fact suggests, that if an older person is believed fit for surgery then a standard surgical procedure with primary anastomosis can be tolerated without excess surgical and anastomotic complications. On the other hand, some reports suggest that patients with more comorbid conditions could have more pre-operative complications and a higher mortality risk [15,16], but clinically healthy patients have results similar to those of younger patients [17].

The European Organization for Research and Treatment of Cancer (EORTC) Elderly Task Force experts recommended that older patients with advanced stages of colorectal cancer should not be denied adjuvant chemotherapy or neoadjuvant radio-chemotherapy, only on the basis of chronological age. Treatment decisions should take into account the estimated absolute benefit, life expectancy, treatment tolerance, cognition, comorbidities, and patient preferences [8].

On the other hand, Guidelines from the US National Comprehensive Cancer Network recommend use of a Comprehensive Geriatric Assessment (CGA) to guide decision making when considering chemotherapy in elderly patients [18,19]. However, there currently exists no evidence-based method to combine the many data items generated by the CGA into one decision about whether to offer chemotherapy or which regimen to use [20]. As shown in previous reports [5], our patients were undertreated: there were significant differences between patients below 75 years and patients above 75 years concerning radio or radiochemotherapy for rectal cancer and chemotherapy for colic cancer.

## CONCLUSION

Colorectal cancer in elderly patients is characterized by a high rate

of emergent presentations, of post-operative non-specific complications and a high post-operative mortality. In comparison with patients below 75 years, elderly colorectal patients are undertreated, mainly because of their age and not because of their tumour type or comorbidity. Surgery is feasible and can be safe for this category of patients but it needs much more evaluation of comorbidities, per and post-operative intensive care to avoid post-operative non-specific complications.

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