Survival Rates among Elderly Population with Advanced Colorectal Cancer in Saudi Arabia

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ABSTRACT

Introduction: Colorectal cancer (CRC) is one of the most common causes of cancer-related mortality. Previous studies conducted in Saudi Arabia and provided information about the current situation regarding CRC but still, no enough data was found about the elderly population. ***Objectives:*** *We aim to evaluate the overall survival of advanced CRC patients in the elderly population and to assess treatment tolerance.* ***Methods:*** *We conducted a retrospective analysis for the medical records department at Princess Norah Oncology Center (PNOC), King Abdulaziz Medical City, Jeddah, Saudi Arabia. We included patients treated at PNOC in the period between 2010 and 2015. Only patients aged above 70 years old with the advanced colon.* ***Results:*** *We included 57 cases with advanced colon cancer in our final analysis. For all the patients in this cohort study, the average age of diagnosis was 76.51 ± 9.28 years, and 71.93% were males. Overall 1-year, 2-year, and 5-year survival rates were 84.3%, 72%, and 54%, respectively. Survival analysis suggested surgical treatment, local radiation, younger ages, recurrent patients, female patients, and Non-mucinous Adenocarcinoma were associated with better survival. Multivariate Cox regression analysis showed that younger age (HR: 1.05, 95%CI=1.00-1.11, p-value=0.050), surgical treatment (HR: 0.15, 95%CI=0.04-0.60, p-value=0.007) and local radiotherapy (HR: 0.04, 95%CI=0.00-0.70, p-value=0.027) were significantly associated with longer survival. Newly diagnosed patients, males and mucinous adenocarcinoma were associated with shorter survival with no statistically significant difference.* ***Conclusion:*** *Survival rates among outpatients were higher than previous local studies. 5-year survival rate was 54%. Survival and regression analysis showed younger age, surgical treatment and local radiotherapy were significantly associated with longer survival.*

Keywords: CRC, Colorectal cancer, Survival rates, Elderly, Saudi Arabia

Abbreviation: PNOC: Princess Norah Oncology Center; CRC: Colorectal Carcinoma; IRB: Institutional Review Board

INTRODUCTION

Colorectal cancer (CRC) becomes a major burden on the healthcare system worldwide. CRC ranked the fourth leading cause of cancer-related mortality. It is estimated by 2030 CRC incidence will be 2.2 million cases with 1.1 million deaths [1]. Adenocarcinoma is the most common histopathology in large bowel besides being the second cause of deaths worldwide [2].

CRC prognosis depends mainly on tumor stage at the time of diagnosis. 30% of patients have distant metastases at diagnosis time. 50% of patients develop recurrence and metastases [3]. Many treatment lines developed over the past decades to improve CRC survival including surgical treatment for early stages, systemic chemotherapy as folinic acid, fluorouracil, and oxaliplatin (FOLFOX4) regimen and folinic acid, fluorouracil, irinotecan (FOLFIRI) which improved overall survival with advance in the field of molecular biology as competitive inhibitor of epidermal growth factor receptor (EGFR) [4,5].

Incidence of CRC increase with age, 70% of CRC cases found above 75 years [6]. Management of elderly patients poses

a challenge [7]. This is attributed to multiple factors as associated Comorbid conditions including the cardiovascular system, presence of liver diseases and peritoneal disease which make surgery outcomes [8]. Another challenge is chemotherapy administration which had more toxicity and the need for frequent hospitalization [9]. Besides shorter life span this may affect physician choice to give chemotherapy. A SEER study showed elder patient less likely to get chemotherapy [10]. However an observational study showed capecitabine, first-line chemotherapy, had an overall survival of 22.6 months with good tolerability [11]. A systematic review of observational studies concluded age was not related to overall survival and the result was inconsistent in the included studies [12].

In Saudi Arabia, According to Saudi Cancer Registry (SCR), CRC is the most common cancer in males and the third most common cancer in females, with a median age at diagnosis of 59 and 58 years among males and females, respectively. Although the majority of CRC cases present at a relatively early stage (23.3%, localized; 42.7%, regional), a substantial number of cases involve distant metastasis (25.9%). With respect to the older demographic, CRC is leading cancer in males above 60 and females above 75 [13].

A retrospective analysis of the Saudi Cancer Registry's data, conducted between the years 1994-2010, found that the overall 5-year survival rate for CRC was 44.6% between the years 1994-2004; survival data for the period 2005-2010 was insufficient. Moreover, the data analyzed was not specific to the elderly population. The chemotherapy regimens used and the patients' tolerance to treatment were not reported [14].

Our aim is to evaluate the overall survival of advanced CRC patients in the elderly population and to assess treatment tolerance. To our knowledge, this is the first study to evaluate such concerns in Saudi Arabia.

MATERIALS AND METHODS

Study Setting

The study retrospectively collected the data from the medical records department at Princess Norah Oncology Center (PNOC), King Abdulaziz Medical City, Jeddah, Saudi Arabia.

Study Subjects

All colonic adenocarcinoma patients treated at PNOC between 2010 and 2015 were considered. Only patients aged above 70 years old with advanced colon cancer (stage IV) or an unrespectable early stage were included. The exclusion criteria were; patients with other malignancies in the last five years, patients undergoing neoadjuvant therapy and patients at early stages (0 to III).

Sampling and Study Design

This is a retrospective cohort study following a convenience sampling technique where all patients fitting the inclusion criteria were included.

Data Collection and Management

The information about colorectal carcinoma (CRC) patients was collected through structured data collection sheets. The medical records of patients admitted between January 2010 and December 2015 were used. The information was extracted using the electronic patient record systems (BEST CARE and Quadramed) and health records. Serial numbers were used instead of names to consider confidentiality.

Ethical Considerations

Institutional review board (IRB) approval was obtained prior to data collection. Data were concealed with access granted only to investigators and security codes were given to every patient.

Statistical Analysis

Descriptive statistics to summarize patients' characteristics were presented in the form of mean and standard deviation for continuous variables while categorical variables were presented in the form of frequency and percentage. Chi^2 test (or Fisher's test, as appropriate) was used to compare categorical variables, while Student's t-test (or Mann-Whitney test, as appropriate) was used to compare the continuous variables. Kaplan Meier analysis in the form of survival curves was used to present the survival probabilities of each group and a log-rank test was used to compare their survival.

A multivariate Cox regression analysis of overall survival was used to identify all possible prognostic factors affecting the survival of PCL patients. Moreover, we computed the hazard ratios from the generated model coefficients to make it easily interpretable. All analyses were two-sided considering p-value <0.05 as statistically significant and were conducted by using R version 3.2.5 software.

RESULTS

Patient Population and Baseline Characteristics

After applying the inclusion and exclusion criteria, our study cohort was finalized with 57 cases. For all the patients in this cohort study, the average age of diagnosis was 76.51 ± 9.28 years, and 71.93% were males (Table 1). About 67% of the patients were of a new-onset and the rest we presenting with recurrence. Moreover, most of the patients (87.72%) have a non-mucinous adenocarcinoma and performed surgery (80.70%) at least once as a treatment modality. Regarding medical treatment, 40 patients used first-line treatment with subsequent use of second-line treatment in 23 patients and the third in nine of them. In contrast, only 12.28% of the patients treated with local radiotherapy and 7.01% with local liver ablation. On comparing different characteristics among alive and dead patients in the study a significant difference only found in histological subtype and going through the first line of treatment. All currently dead patients were diagnosed with non-mucinous adenocarcinoma compared to 81.08% in the living ones. In the same context, only 50% of the dead patients used first-line treatment compared to 81.08% of the living ones (Table 1).

Table 1 Basic characteristics of included patients

Outcomes		Alive		Dead		Total		p-value
		N	%	N	%	N	%	
Age: Mean (SD)		75.41 (8.207)		78.55 (10.94)		76.51 (9.28)		0.269 ¥
Gender	Female	10	27.03%	6	30%	16	28.07%	0.812
	Male	27	72.97%	14	70%	41	71.93%	
Diagnosis	New Diagnosis	25	67.57%	13	65%	38	66.67%	0.844
	Recurrence	12	32.43%	7	35%	19	33.33%	
Histological subtype	Mucinous Adenocarcinoma	7	18.92%	0	0%	7	12.28%	0.045* ¶
	Non-mucinous Adenocarcinoma	30	81.08%	20	100%	50	87.72%	
Surgery	No	6	16.22%	5	25%	11	19.3%	0.491 ¶
	Yes	31	83.78%	15	75%	46	80.7%	
First-line Treatment	No	7	18.92%	10	50%	17	29.82%	0.014* ¶
	Yes	30	81.08%	10	50%	40	70.18%	
Second-line Treatment	No	19	51.35%	15	75%	34	59.65%	0.082
	Yes	18	48.65%	5	25%	23	40.35%	
Third-line Treatment	No	30	81.08%	18	90%	48	84.21%	0.471 ¶
	Yes	7	18.92%	2	10%	9	15.79%	
Local Radiotherapy	No	31	83.78%	19	95%	50	87.72%	
	Yes	6	16.21%	1	5%	7	12.28%	
Local Liver Ablation	No	33	89.19%	20	100%	53	92.98%	0.705 ¶
	Yes	4	10.81%	0	0%	4	7.01%	

SD: Standard Deviation; * Significant p-value<0.05; ¥: t-Test; ¶: Fisher's exact test

Overall Survival

Overall 1-year, 2-year, and 5-year survival rates were 84.3%, 72%, and 54%, respectively. Kaplan-Meier curve and log-rank testing suggested that patients with surgical treatment (Figure 1), local radiation (Figure 2), younger ages (Figure 3), recurrent patients (Figure 4), female patients (Figure 5) and Non-mucinous Adenocarcinoma (Figure 6) were associated with better survival. However, only surgery showed a statistically significant difference when testes with the log-rank test (p-value=0.031).

These findings were also consistent with the results of the multivariate Cox regression analysis. It showed that younger age (HR: 1.05, 95%CI=1.00-1.11, p-value=0.050), surgical treatment (HR: 0.15, 95%CI=0.04-0.60, p-value=0.007)

and local radiotherapy (HR: 0.04, 95%CI=0.00-0.70, p-value=0.027) were significantly associated with longer survival. On the other hand, newly diagnosed patients, males and mucinous adenocarcinoma were associated with shorter survival. However, none of these variables showed any statistically significant difference compared to the reference value (Table 2).

Table 2 Multivariate Cox regression analyses of overall survival

| Parameters	HR [95% CI]	p-value
Age	1.05 [1.00,1.11]	0.050*
Histopathological Subtype		
Mucinous Adenocarcinoma	Reference	
Non-mucinous Adenocarcinoma	0.63 [0.23,0.83]	0.998
Diagnosis		
Recurrence	Reference	
New Diagnosis	1.68 [0.61,4.58]	0.313
Gender		
Female	Reference	
Male	1.04 [0.39,2.78]	0.945
Surgery		
No surgery	Reference	
Surgery	0.15 [0.04,0.60]	0.007*
Local Radiotherapy		
No local Radiotherapy	Reference	
Local Radiotherapy	0.04 [0.00,0.70]	0.027*
*Significant p-value<0.05		
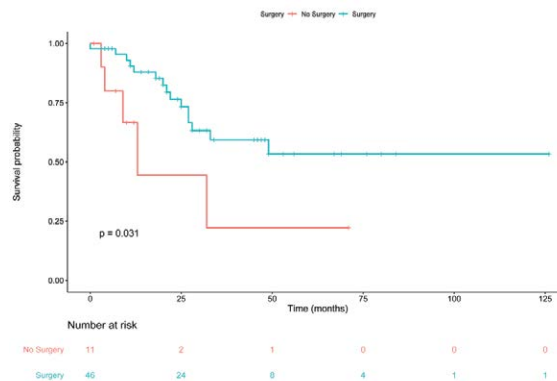
Figure 1 The Kaplan-Meier estimates of survival for surgical treatment (with log-rank test)
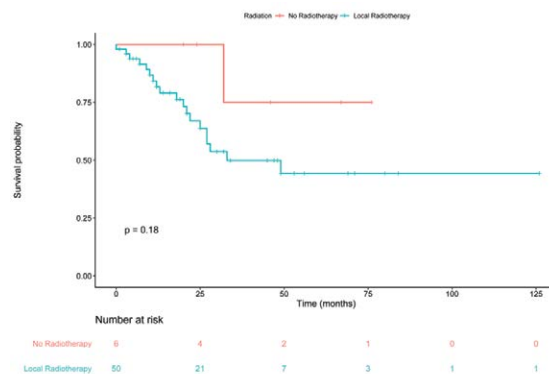

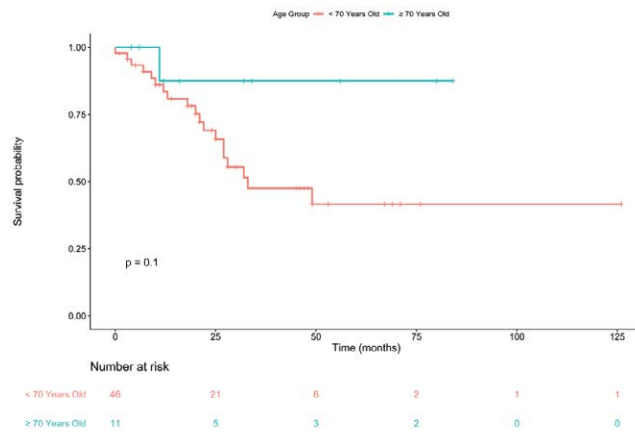**Figure 2 The Kaplan-Meier estimates of survival for local radiotherapy (with log-rank test)**

Figure 3 The Kaplan-Meier estimates of survival for patients' different age groups (<70 years old and ≥ 70 years old) (with log-rank test)
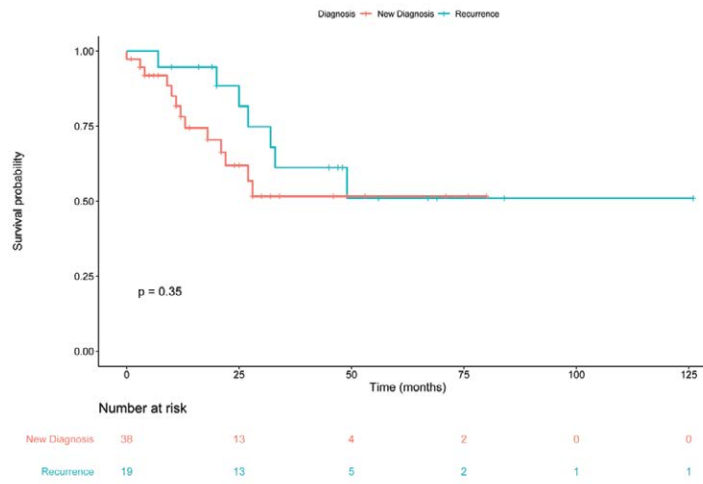

Figure 4 The Kaplan-Meier estimates of survival for diagnosis (with log-rank test)
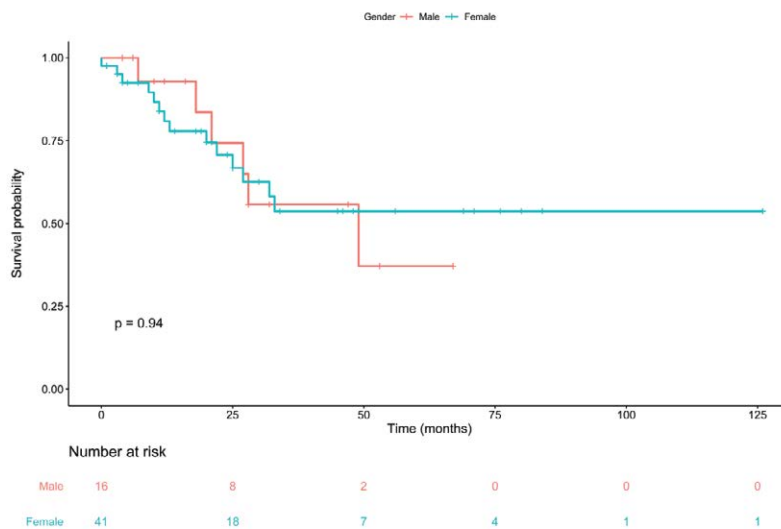

Figure 5 The Kaplan-Meier estimates of survival for patients' gender (with log-rank test)
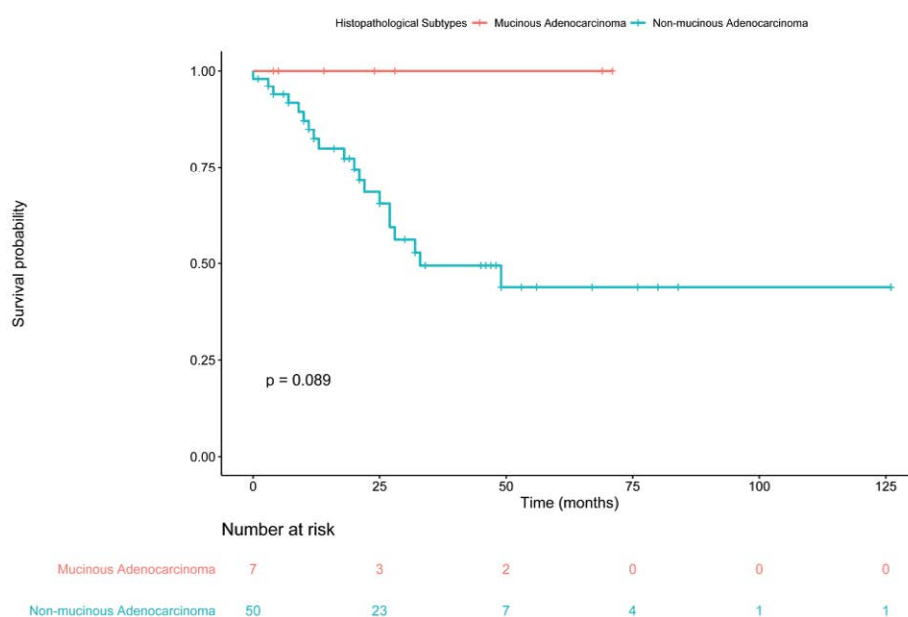
Figure 6 The Kaplan-Meier estimates of survival for histopathological subtypes (with log-rank test)

DISCUSSION

This is a retrospective analysis of the medical records department at Princess Norah Oncology Center (PNOC). The mean age of included patients was 76.51 years old and 71.93% were males. 5-year survival rate was 54% between 2010 and 2015. Regression analysis showed younger age, surgical treatment and local radiotherapy were significantly associated with longer survival.

The estimated 5-year survival rate was higher than the survival rates reported in the period 1994-1999 and 2000-2004 in Saudi Arabia which was 44.7% and 44.3% respectively [14]. Another study in Saudi Arabia showed a 5-year survival rate was 39% in the period between 1990-1998 after curative treatment for rectal cancer [15]. 5-year survival rate in some Asian countries was 77% in China [16], 31.2% in India [17], 57.0 to 58.9% in Singapore [18], 41 to 61% in Korea [19] and 40.4 to 45.4% in Malaysia [20]. 5-year survival rate was 65.9% in the United States in the period between 2002-2008 [21].

Our result showed female patients had longer survival. The previous local study concluded the same and explained these results by females have a lower threshold for their health condition and seek medical help earlier leading to early detection and hence better survival [14]. Besides females, in general, had lower comorbid conditions especially the cardiovascular system leading to better tolerability of treatment [8]. However, survival data from the United States showed no difference in survival rates between males and females patients [21]. Data from SEER analysis showed males and females have similar comorbid conditions [22].

Our findings suggest that local radiotherapy and surgical treatment improve survival. Surgical resection usually needed to prevent bowel obstruction and prevent blood loss. The study showed tumor resection in elder patients shorten survival rates due to associated comorbid diseases which have a negative impact on surgery outcome [8]. A retrospective analysis of SEER databases concluded the same [22].

Younger age was associated with longer survival. This is similar to results reported by a systematic review which showed consistency in included studies that reported younger age had longer survival and explained it by younger patients tend to have more aggressive treatment but this review included a wide range of age groups [12].

Our study provides a comprehensive view of the elder population with advanced colorectal cancer regarding their survival rates, and tolerance for treatment modalities. However, the data is limited by small sample size, only 57 cases met our inclusion criteria. Our results depend on data obtained from medical records which may be subjected to biases and inaccurate information. We recommend larger studies to address these issues with larger sample size.

CONCLUSION

Survival rates among outpatients were higher than previous local studies. 5-year survival rate was 54%. Survival and regression analysis showed younger age, surgical treatment and local radiotherapy were significantly associated with longer survival.

DECLARATIONS

Conflicts of Interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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