SURGICAL MANAGEMENT OF COLORECTAL CARCINOMA: CLINICAL FEATURES AND OUTCOMES AT A TERTIARY CARE HOSPITAL

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ABSTRACT

Objective: To present our experience about the surgical management and short-to-mid-term outcome of patients with colorectal cancer with an emphasis on the implications for our local population.

Methodology: This was a descriptive study conducted between July 2010 to June 2015. We included adult patients with a diagnosis of colorectal cancer who were managed surgically and they were followed-up post-operatively for up to 12 months. Patients demographics, clinical features, radiological and pathological staging, surgical intervention performed, early postoperative complications, mortality and recurrence data was obtained.

Results: A total of 81 patients were studied with a mean age of 50.25 \pm 4.71 years. The average follow up duration was 6.56 \pm 2.76 months. Among the 67 cases of adenocarcinoma, 15 (22.4%) were grade 1 tumours, 24 (35.8%) were grade 2 tumours while 28 (41.8%) were grade 3 tumours. Adenocarcinoma most frequently presented during Stage C1 (n =23, 34.3%) which was followed by 22 (32.8%) cases of stage B tumours. Squamous cell carcinoma presented during stage C2 (n =8, 57.1%) which was followed by stage C1 (n =4, 28.6%). The median survival duration during the follow-up period was 11 months (95% CI, 9.25 to 12.74).

Conclusion: Colorectal carcinoma involved younger age groups in our society with frequent late presentation. Early clinical presentation was associated with best overall and recurrence free survival while presentation at later stages of disease lead to shorter survival and early recurrence.

Key Words: Colorectal cancer, Surgical management, Outcome, Recurrence

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INTRODUCTION

Cancer has become one of the major form of non-communicable diseases (NCD) over the last two decades and is increasing in incidence within the low and middle-income countries (LMICs)¹. The GLOBOCAN 2012 estimates show that colorectal cancer (CCa) is the 3rd most commonly diagnosed cancer worldwide with 1.36 million new cases each year and it is rapidly rising in the LMICs due to increasing trend towards tobacco use, obesity and other risk factors¹. The World Health Organisation (WHO) country health profile for Pakistan shows that incidence of CCa is increasing with age standardised incidence rate (ASR) of 3.1 per 100,000 persons per year for males while it is 5.1 per 100,000 persons per year for females². This trend is rapidly increasingly as reported by Bhurgri et al³, with a 41% increase of CCa in males during a 5-year period. Studies have also shown

that in Pakistan CCa occurs at a significantly younger age (46.5 years to 54 years) as compared to the rest of the world^{4,5}.

The above epidemiological facts show that higher clinical vigilance, improved surgical care and close post-operative follow-up is of utmost importance in order to reduce the impact of morbidity and mortality due to colorectal cancer. Multiple guidelines have been developed over the course of time in order to standardize the optimal management of patients with CCa and hence to improve the outcomes^{6,7}. Good epidemiological and clinical knowledge is of the essence in order to achieve better clinical results in cancer patients especially in the non-oncologist physicians and surgeons.⁸ Unfortunately, there are very limited resources available in our country to keep track of cancer patients during follow-up and data about survival, disability and mortality is largely based on limited cancer registries.^{9,10}

To reduce the gap between the clinical management of CCa patients and its impact on public health due to the reduced availability of population data, it is imperative that new data is constantly provided in the form of hospital based research and smaller cancer registry analysis.

We, therefore, aimed to present a comprehensive analysis of the surgical management of CCa with an emphasis on demographics, clinical features, surgical procedures, complications and short-to-mid-term outcome in terms of recurrence and early postoperative mortality. Local recurrence by the stage, effect of tumour stage on survival, differences in survival distribution and relation of stage with survival distribution are important areas of emphasis. This would help understand our local patterns of CCa prevalence and the effectiveness of surgical strategies for management of these patients.

METHODOLOGY

This descriptive study was conducted at the Department of General and Laparoscopic Surgery, Pakistan Institute of Medical Sciences, Islamabad between July 2010 and June 2015. Approval was obtained from the hospital ethical committee and informed consent was taken from all patients before inclusion in the study. Convenience sampling was done. All patients with a diagnosis of colorectal carcinoma above the age of 16 years irrespective of gender, mode of presentation and tumour stage and grade were included. Patients who did not consent to surgical intervention for their disease, those with surgical or malignancy related complications of already operated tumours and those who failed to follow-up post-operatively for at least the initial thirty days were excluded. Data was collected about patient demographics, predominant clinical features, mode of presentation, radiological and histopathological features, surgical procedures employed, early postoperative complications, follow-up duration, recurrence and mortality. The histopathological features recorded were tumour type, tumour grade and stage of the tumour according to Dukes staging system⁶.

The surgical procedure was tailored to individual patient requirements especially taking into consideration the location, clinical stability and overall resectability/stage of the primary lesion. Those patients who presented with advanced stage disease were offered palliative surgical procedures after complete clinical evaluation and if the patient agreed, they were operated accordingly. Similarly, patients who presented with emergent clinical problems due to obstruction or perforation were initially intervened with the least invasive and most rapid method of bowel decompression and diversion and later on, once the patient was optimised, only then the definitive procedure was undertaken.

Postoperative mortality was defined as mortality that occurred within 30 days of the operation for bowel cancer. Mortality that occurred during the follow-up period after the first 30 days was termed late mortality. Anastomotic leak was defined as spillage of bowel contents intraperitoneally which necessitated intervention in the form of a laparotomy local drainage and closure methods. Recurrence was defined as documented local or distant disease appearance after initial complete resection. All postoperative complications were graded according to the Clavien-Dindo classification of postoperative complications. Data was recorded in a Microsoft Excel chart for each patient with a unique identifier and was later analysed using SPSS version 22. Frequency was calculated for gender, presenting features, operative features, surgical procedures done, palliative procedures done, histopathology features and stage of disease, postoperative complications, recurrence and mortality. Significance testing was done using chi-square or Fischer's exact test. The cut-off value for statistical significance was kept at <0.05. Kaplan-Meier survival analysis, log rank test and pairwise log rank analysis were done to see effect of tumour stage on survival, differences in survival distributions, and relation of stage with survival distribution respectively.

RESULTS

A total of 81 patients were operated during the five-year period with 49 males and 32 females in a ratio of 1.53:1. The mean age was 50.25 \pm 4.71 years. The average duration of symptoms to the time of presentation was 5.7 \pm 2.30 months while the average follow up duration was 6.56 \pm 2.76 months. The detailed clinical and operative features and their frequencies are shown in Table 1 & Figure 1.

Among the 67 cases of adenocarcinoma, 28 (41.8%) were grade 3 tumours; similarly, among the 14 cases of squamous cell carcinoma, 7 (50%) were grade 2 tumours as shown in Table 2.

Among grade 2 tumours (n = 31), there were 4 (33.3%) recurrent cases while in grade 3 tumours (n = 34) the remaining 8 (66.7%) of recurrent cases occurred. Late mortality occurred in 8 (30.8%) of grade 2, 16 (61.5%) in grade 3 and only 2 (7.7%) in grade 1 tumours. On chi-square analysis, higher grade was significantly associated with late mortality (p = 0.032), Table 3.

Adenocarcinoma most frequently presented during stage C1 (n =23, 34.3%) which was followed by 22 (32.8%) cases of stage B tumours. Stage C2 was encountered in 14 (20.9%) of adenocarcinoma while stage D was encountered in only 8 (11.9%) of cases. Similarly, squamous cell carcinoma presented during stage C2 (n =8, 57.1%) which was followed by stage C1 (n =4, 28.6%) and stage B (n = 2, 14.3%). This shows that squa-

Table 1: Clinical features and operative findings

Clinical Features		Frequency	Percentage	
Gender	Male	49	60.5%	
	Female	32	39.5%	
Presenting Features	PR Bleed	44	54.3%	
	Change in Bowel Habits	51	63.0%	
	Weight Loss	47	58.0%	
	Acute/Subacute obstruction	26	32.1%	
	Perforation	5	6.2%	
	Comorbids	17	21.0%	
	Bowel Segment			
	• Colon	50	61.7%	
	• Rectum	31	38.3%	
Operative Features	Colon Segment			
	Ascending Colon & Caecum	14	28.0%	
	Hepatic Flexure	8	16.0%	
	Transverse	6	12.0%	
	Splenic Flexure	8	16.0%	
	Descending Colon	7	14.0%	
	• Sigmoid	7	14.0%	
	Rectum			
	High Recto-sigmoid	23	28.4%	
	Low Rectum	13	16%	
Surgical Procedures	Open Right Hemicolectomy	21	25.9%	
	Laparoscopic Right Hemicolectomy	6	7.4%	
	Open Left Hemicolectomy	13	16.0%	
	Laparoscopic Left Hemicolectomy	6	7.4%	
	Anterior Resection	23	28.4%	
	Abdominoperial Resection	9	11.1%	
	Laparoscopic Abdominoperial Resection	4	4.9%	
Palliative Procedures		9	11.1%	

Table 2: Histopathological features

Feature		Frequency	Percentage
Histological Type	Adenocarcinoma	67	82.7%
	Squamous Carcinoma	14	17.3%
Tumour Grade	Well differentiated (G1)	23	28.4%
	Moderately differentiated (G2)	29	35.8%
	Poorly differentiated (G3)	29	35.8%
Dukes Stages	Stage B	24	29.6%
	Stage C1	27	33.3%
	Stage C2	22	27.2%
	Stage D	9	11.1%

Table 3: Outcome variables

Variables	Frequency	Percentage
Postoperative Complications		
Wound Infection	10	12.3%
Anastomotic Leak	4	4.9%
Chest Infection	7	8.6%
Sepsis	4	4.9%
Metabolic Abnormalities	5	6.2%
Recurrence	12	14.8%
Mortality	9	11.1%

Fig 1: Distribution of clinical features for colonic and rectal carcinoma

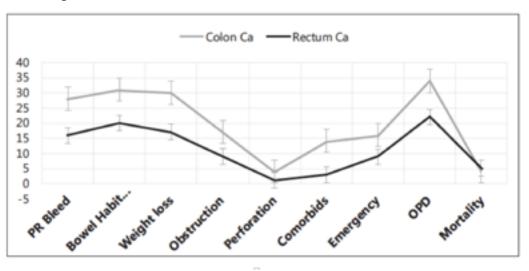
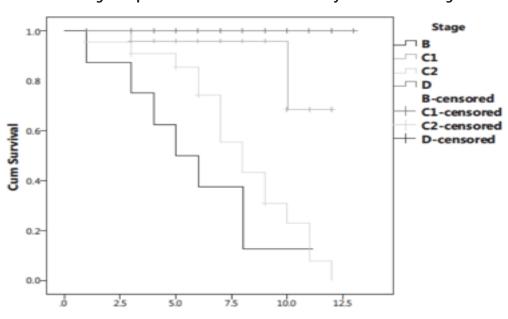


Fig 2: Kaplan-Meier survival function analysis for tumour stage



mous cell carcinoma usually presents relatively late as compared to adenocarcinoma (p = 0.033).

The tumors stage was plotted against recurrence and late mortality and it was found that Dukes C2 stage was the most commonly recurrent tumours (n =8, 66.7%) while 4 (33.3%) of stage C1 tumours recurred during the follow-up. There were no recurrences for stage B tumours (n =24). Stage C2 tumours were most commonly associated with late mortality (n =16, 61.5%) which was followed by stage D with 7 (26.9%) cases of late mortality. Stage C1 was associated with 11.5% (n =3) cases of late mortality. Stage D tumours were frequently managed using palliative procedures and their late mortality was noted to reach 77.8% during the follow-up period.

The data was sorted according to the portion of the bowel involved (colon vs. rectum) and the clinical features are plotted for the two entities in Figure 1. Patient age (Mann-Whitney U: 224, Z =-1.51, p =0.13) and symptoms duration (Mann-Whitney U: 242, Z =-1.24, p =0.21) were not statistically different for mortality. Moreover, mortality was not affected by the bowel portion involved (U: 261, Z =-1.13, p =0.26) neither by the histological nature of the tumour (U: 306, Z =-0.41, p =0.68).

Kaplan-Meier survival analysis was conducted to compare the tumour stage and its effect on the overall survival. Although there were a high number of censored cases, the overall median survival time was recorded to be 11 months (95% CI, 9.25 to 12.74). A log rank test was conducted to determine if there were differences in the survival distributions for the different tumour stages. The survival distributions for the tumour stages were significantly different (p <.0005). Pairwise log rank comparisons were conducted to determine which tumour stage had different survival distributions. There was a statistically significant difference in survival distributions for stage D vs. stage B (p<0.0005); stage D vs. stage C1, (p < 0.0005). However there was no significant difference of survival distribution between stage D vs. stage C2 (p =0.25). Similarly, survival distribution for stage C2 was significantly different when compared to stage B (p < 0.0005) and stage C1 (p < 0.0005). However, no significant survival distribution difference was noted between stage C2 vs. stage D (p =0.25). Details are shown in Figure 2.

DISCUSSION

In Pakistan, exact figures for incidence, prevalence and time trends are unavailable due to lack of large population based cancer registries, however, one instance of a small cancer registry is the South Karachi Cancer Registry (SKC)⁹. The utility of this registry, though hampered by the small size of population it serves, however, due to the ethnic and racial variability of this area, may

be representative up to a good extent for overall population of the country³. This lack of large cancer registries has led to the publication of numerous hospital based literature with particular emphasis on epidemiology^{5,11-13}. CCa clinical features have been explained by many studies in our local population and several clinical and epidemiological studies have shown that although its incidence is low as compared to developed countries, the worrying feature is its occurrence in lower age groups and presentation at advanced stage which lead to disability of a potentially functioning age groups of the community^{4,10,14}. This emphasises the importance of implementation of regular screening strategies and establishment of large population based cancer registries in order to reduce morbidity and mortality by instituting timely diagnostic and therapeutic services^{3,5,14}.

Literature suggest that although there have been tremendous advancements in the understanding of CCa over the last 20 years, the overall survival is only between 32%-64%. Studies by Xynos et al⁷, Dotan et al¹⁵ and Borie et al¹⁶ suggest that CCa management differs between hospitals and surgeons. Numerous treatment guidelines have been developed in order to optimise the outcome with uniform practice parameters. However, patient involvement, establishment of multidisciplinary teams and good surgical expertise can all help in improving these outcomes 17-19. In a cohort of colorectal cancer patients less than 75 years of age, Veen and co-workers²⁰ have analysed the long-term survivorship and concluded that approximately one third of patients die of CCa with disease specific risk factors such as overall stage and nodal status. On the other hand, in a retrospective review of elderly patients Tan and associates²¹ have concluded that outcome in CCa patients who are above the age of 80 years is primarily determined by age, emergent nature of surgery and Charlson comorbidity index of above 3. Additionally, they have reported that long-term survival is dependent upon the stage as well as any preoperative complications of the disease itself. Survival with particular emphasis on the preoperative risk factors for prognosis are detailed in a Danish study by Iversen²². According to Iversen there is a notable improvement in early postoperative survival from 86%-90% in the late 70s to 94% during late 90s. Similarly, it has been reported that postoperative mortality after emergency colorectal cancer surgery is higher. Another important aspect for colorectal surgeons is to consider the delay between diagnosis and operation as it has been stated that a delay of 60 days or more affect the outcomes negatively. The 5-year survival after acute curative surgery for CCa is very low²².

In the present study, we noted that almost one third of colon cancer involved the right side of the colon, including caecum, ascending colon, hepatic flexure and the right one third of transverse colon. This rightward shift of colon cancer was previously reported in the literature especially in a large multicentre survey by Beart et al²³ in 1995. Similar findings have also been reported by Shaikh et al⁵ where they noted 51.6% cases of right sided disease. In the same study by Shaikh AJ et al⁵, other patient demographics, such as age and gender distribution were also in agreement to our findings (mean age 54.22 ±14 years vs. 50.25 ±4.71 years and male to female ratio 1.58:1 vs. 1.53:1), verifying that these clinical features and demographics remains largely similar across the country.

Tumour characteristics in our study were compared with some local studies. In a study by Khan et al²⁴, about 97% of tumours were adenocarcinomas which was quite high but in agreement with our study where we noted 82.7% cases of adenocarcinomas and 17.3% cases of squamous cell carcinoma. Similarly, we noted 38.3% cases of rectal tumours while in the above mentioned study, rectal tumours were noted in 37.7% of cases. Bowel portion involvement has been taken into consideration in numerous studies as it was suggested that rectal cancers were associated with higher morbidity and mortality as compared to colonic tumours^{25,26}. However, in a recent study by Nedrebo et al²⁷, it has been shown that survival for rectal cancer changes over time due to various factors such as early detection and good curative surgery techniques especially the sphincter preserving techniques. We noted that outcomes in terms of mortality and postoperative complications were similar and were not affected by the location of the tumour in either colon or rectum. Our findings of similar outcome for rectal and colonic tumours could be due to shorter follow-up times where majority of patients were lost to follow-up after the initial 6-months. Another factor to be considered in outcome assessment should be the assessment of quality of life which is difficult to assess and interpret due to involvement of multiple personal, social and economic factors^{28,29}.

We noted that majority (60.5%) of patients presented in Duke's Stage C which was followed by stage B (29.6%) and then stage D (11.1%). These findings are largely similar to the findings by Khan MR et al²⁴ where stage C was found in about 42.8% of patients, which was followed by stage B in 33.6% while stage D was found in 5.1% of patients. Preoperative staging is important to know the extent of bowel and/or metastatic spread which effectively lead to change in management decisions as well as a difference in postoperative survival. Khan et al³⁰ in a study evaluated the survival benefits of management of advanced CCa especially the role of metastasectomy. They demonstrated that metastasectomy has favourable results on overall survival up to the age of 85 years (hazard ratio, 0.68-0.72, p < 0.0001). Although we did not record the number, site and size of metastasis, our observation was that curative metastasectomy and/

or palliative procedures do provide good symptoms management and it can improve outcomes in our setup despite the fact that patients have little resources available for postoperative rehabilitation. Higher rates of late mortality in patients undergoing palliative procedures might largely be due to multiple factors which become established in late presented patients. We, therefore, noted that there was a strong association between advanced stage disease requiring palliative procedures and high mortality postoperatively (p = 0.004,). We also could not establish significant association of a particular procedure and late mortality, although the hand assisted laparoscopic (HAL) techniques were prolonged but associated with low rates of early postoperative complications.On survival analysis, we noted that an advanced stage was strongly associated with lower overall survival (median: 11 months, 95% CI, 9.25 to 12.74). It is important to note that overall survival did not change beyond late Stage C (stage C2) and recurrent disease was higher in these patients. In our patients about 32.1% (n = 26) died within the first 12-months, however, these results are far from the conclusion as many patients were lost to follow-up after the initial 6 months. Sjovall et al³¹ has shown that crude survival rates were 46.2% during 5-year period. This is comparable to our 67.9% survival rates during the 12-month period as mortality increases with time for tumours of late stage C and above, as shown in Figure 2.

LIMITATIONS

The limitations of this study are small sample, shorter and variable time of follow-up, lack of important outcome data due to patients loss to follow-up and no data about the outcome once adjuvant treatment was instituted. These weaknesses can be improved by including large number of patients for a longer duration of follow-up in a multidisciplinary team environment. Further research is warranted in order to better understand our local epidemiological trends, clinical outcomes and to evaluate the value of early screening programs.

CONCLUSION

Colorectal carcinoma involved younger age groups in our society with frequent late presentation. Early clinical presentation was associated with best overall and recurrence free survival while presentation at later stages of disease lead to shorter survival and early recurrence. Good surgical management is associated with better outcome while most of the postoperative complications occur within the initial stay at the hospital.

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CONTRIBUTORS

SAS conceived the idea, planned the study and drafted the manuscript. SHW and AM helped acquisition of data, did statistical analysis and critically revised the manuscript. All authors contributed significantly to the submitted manuscript.