RESEARCH COMMUNICATION

Demographics, Pathologic Patterns and Long-term Survival in Operable Colon Cancers: Local Experience in Pakistan

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Abstract

Background: Colon cancer is a common malignancy with its incidence reportedly rising in Asian Countries, including Pakistan. There are no comprehensive data available from Pakistan which focus on associations of various factors with long-term survival of colon cancer. We therefore present an analysis of findings from our centre. Methodology: In this retrospective study adult patients with colon cancer diagnosed through 2000-2003 were included. A comprehensive questionnaire was filled for each individual through review medical and pathology reports. Long term survival data was collected from contactable patients or their relatives. Results:A total of 93 patients were assessed, 57 males and 36 females (M: F= 1.58: 1). Mean age of diagnosis was 54 years. Of the total, 49.5% of the patients had right sided (mortality rate 51.6%), 10.8% had transverse colon, (mortality rate 37.5%), 7.5% had descending colon (mortality rate 66.7%) and 32.2% had sigmoid colon (mortality rate 40.9%) cancers. Stage I disease on diagnosis was found in 16%, stage II in 42.7 (mortality 40 %) and stage III in 41.3% (mortality 70 %). Tumors were well differentiated in 20.2% (mortality 42.9%), moderately differentiated in 61.9% (mortality 43%) and poorly differentiated in 17.9%(mortality 70%). In 36.3% of the patients less than 12 lymph nodes were removed (mortality 55% Vs 43% in patients with > 12 lymph nodes removed). Margins were free in most patients but a radial margin was reported in only 44%. Most patients had pure adenocarcinoma while a mucinous type differentiation was seen in 19.7%, 3% had signet ring morphology, 1.5% adeno-squamous carcinoma and similar number with neuroendocrine differentiation. Overall 5 year all cause mortality for all stages combined was 46.9%. Conclusion: Colon cancer in Pakistan commonly presents at an advanced stage, there is a male preponderance, and relatively mean younger age at presentation for males is seen. Advanced stage and lymph node involvement along with poorly differentiated pathology, signet ring or mucinous morphology, location in descending colon, positive surgical margins and removal of less than twelve lymph nodes are factors associated with poor long term survival. There is a need to reinforce information about colon cancer and larger studies from the region are needed to confirm the factors analyzed here.

Key Words: Colon cancer - tumour characteristics - prognosis

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Introduction

Availability of reliable cancer incidence data is a problem Pakistan still faces, nevertheless, based on incidence reports from various hospital based registries and by far the most authentic cancer registry the Karachi cancer registry (KCR), it is safe to assume that Pakistan is a country with high cancer burden. The Age adjusted annual incidence (ASR) for all cancers based on KCR data is 179.0/100,000 in males and 204.1/100,000 in females. (Bhurgri et al., 2006). The ASR for colon cancer, from a single and limited cancer registry, in Pakistan for males as 3.2/100,000 compared to 5.1/100,000 reported for the rest of the world, for females the ASR is 2.8/ 100,000 compared to 5.2/100,000 for rest of the world(Bhurgri et al., 2000). South Asians living in west are surprisingly reported to have a far higher rate of colorectal cancers compared to even local population, a risk four fold higher than the locals was reported in one report from California.(Jain et al., 2005).

Age, gender, family history of colon or rectal cancer, height, body mass index, physical inactivity, intake of beef, pork or lamb as a main dish, intake of processed meat and alcohol and are considered to be a risk factors for developing colon cancers (Wang et al., 2001; Wei et al., 2004). Low dietary intake of legumes couples with high meat intake in subjects with high body mass index, which could also be a reason for hyper-insulinemia, is also considered to increase colon cancer by threefold (Singh and Fraser, 1998). Efforts have been made, in the setting of randomized control trials targeting at risk population with intervention to alter behavioral patters,

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and have been considered successful and cost effective (Emmons et al., 2005) .

Pathologic stage, histological grade; small vessel (lymphatic or venular) invasion; extramural venous invasion; peri-neural invasion; tumor border configuration, host lymphoid response to tumor, status of surgical margins, and number of lymph nodes removed (Compton, 1999; Swanson et al., 2003; Wang et al., 2008) are considered to be important. Techniques of surgery resulting in higher survival post resection have been proposed such as a 15% survival advantage claimed in a study comparing mesocolic plane surgery with surgery in the muscularis propria plane(West et al., 2008). Data from Pakistan regarding survival from colon cancer following surgery is scarce, and we attempt to describe the pattern that we observed in patients who were diagnosed in operable stage and remained available for the follow up.

Materials and Methods

We followed 93 patients diagnosed between February 2000 and July 2003. Inclusion criteria was restricted to all comers with operable stage (non metastatic) colon cancer, who by availability of valid address and phone number remained contactable.

Histopathological records were reviewed in detail for location of tumor within colon, type of carcinoma, grades of differentiation, surgical margins including radial margins, number of lymph nodes removed, number of lymph nodes involved, lymphovascualr invasion and peri-neural invasion. The American Joint committee staging system (AJCC) was used to stage the disease. Follow-up records, chemotherapy records and dates of last contact were recorded. Data was entered into Microsoft excel spreadsheet. Statistical Package for Social Sciences (SPSS) 16 was used to perform data analysis. Pearson Chi Square test and Fischer's exact test was used to analyses the statistical significance of the differences observed.

Results

A total of 93 patients were assessed, 57 patients were males and 36 females (M: F= 1.58: 1). Age Ranged from 09-86 years with a mean age of 54.22 ±15.93 years. Mean age for males being 52.40 ±16.05 and for females 57.69 ±14.87 years.

A total of 49.5% patients had right sided disease including disease involving the cecum, 10.8% had disease in transverse colon, in 7.5% descending colon was site of the lesion and 32.2% had cancer in sigmoid colon. Stage I was recorded in 16% of the patients, stage IIA in 38.7%, IIB in 4%, stage IIIA in 2.7%, stage IIIB in 22.9%, stage IIIC in 15.7%. Grade I differentiation (well differentiated) was seen in 20.2% of the patients, 61.9% had grade II (moderately differentiated) and 17.9% had grade III (poorly differentiated) pathology. Lymphovascular invasion was seen in 15.7% of the total patients, peri-neural invasion in 7.3% patients and perforation invasion in 10.1%. In 36.3% of the patients less than 12 lymph nodes were removed. In 45.2% of the patients lymph node/s were found to be involved by the disease. In 96.3% of the patients proximal margin was tumor free, close in 2.5% and involved in 1.2%. In 98.8% of the patients distal margin was tumor free and involved in 1.2%. Radial margin was reported in 44% patients and was found to be involved in 12% of the patients. Adenocarcinoma of mucinous type differentiation was seen in 19.7% of patients, 3% had adenocarcinoma with signet ring morphology 1.5% had adeno-squamous carcinoma and 1.5% had adenocarcinoma with neuro-endocrine differentiation. Rest had adenocarcinoma without further differentiation. Overall 5 year all cause mortality for all stages combined and when generalized for having received chemotherapy for appropriate stage was 46.9%.

The associated mortality rate with right sided disease was 51.6%, transverse colon 37.5%, descending colon 66.7% and sigmoid colon 40.9% (p-0.718). The associated mortality rate with Grade –I differentiation was 42.9%, with Grade -II it was 43.6% and G-III was 70.0% (p-0.303). None of the patients diagnosed with stage 1 colon cancer died during the five year follow-up. Mortality rates for stage II 40%, IIIA 50%, IIIB 73.3%, IIIC 75% (p-0.006) as shown in Table 1. In patients lymphovascualr invasion the observed mortality rate was 50% (p-0.548), peri-neural 66% (p-0.446) and perforation 60% (p-0.445). The patient in which less than 12 lymph nodes were removed the observed mortality rate was 55% and it was 43.2% in patients in which 12 or more than 12 lymph nodes were removed (p-0.271). The mortality rate for

Table 1. Mortality According to Stage and Lymph Node Involvement

Parameter	Category	Mortality Rate	P-value
Stage	I	0%	
	II	40%	0.002*
	IIII	72%	
Lymph node involvement			
	Yes	63%	0.023**
	No	37%	

*by Pearson Chi Square test; **by Fisher's exact test

Table 2. Features Associated with a Worse Outcome

Adverse Feature	Mortality rate
Pathology Findings	
Adenocarcinoma (AC)	43.2%
AC + Signet ring	100.0%
AC + mucin	65.5%
Lymphovascular invasion	50.0%
Perforation	60.0%
Lymph Nodes removed	
Less than 12	55.0%
12 or greater than 12	43.2%
Grade of differentiation	
G1- Well-differentiated	42.9%
G2-Moderately differentiated	43.6%
G3- Poorly differentiated	70.0%
Location of Tumor	
Right sided disease	51.6%
Transverse colon	37.5%
Descending colon	66.7%
Sigmoid colon	40.9%

Figure 1. Anatomical Location of the Tumors and Associated Mortality

patients with any number of involved lymph nodes was 63.3% (Table 2).

Discussion

In patients presenting with operable stage colon cancer surgery remains the definitive therapy. Various prognostic factors have been linked to ultimate overall survival. Demographics of the patient, Surgical technique(Le Voyer, Sigurdson et al. 2003; Swanson, Compton et al. 2003), experience of surgeon through volume of surgery (Lane R 1999), distal location of the tumor advanced stage (Mentges and Bruckner 1986) adverse pathologic features such as signet ring cell or mucinous differentiation (Liang, Wang et al. 2006) are some of the factors known to adversely affect the out come of such patients. We are presenting the findings in a limited number of patients from a single centre, still, being a rare report from Southeast Asia it may reflect the trends observed in this part of the world. South Asian population by virtue of their different lifestyle are known to behave differently with the same disease even after migration (Ziegler, Hoover et al. 1993). Our analysis reveals that in our patients male preponderance is noticed with male to female ration of 1.5:1, we find a higher mean age of presentation in females compared to male which is in conflict with data from other studies (Ahmad, Idrees et al. 2005). Proximal disease was the predominant site of cancer with close to 50% patients having cecum or right sided colon affected. The worst out come in descending order of frequency was seen in descending colon, ascending colon, sigmoid and transverse colon (Figure 1). the findings are in keeping with international literature reports with high number of patients (Liang et al., 2006) . Most of our patients were diagnosed with stage II disease 42.7 % closely followed by stage III disease 40.1%, the stage which also demonstrated the worst mortality as shown in Table (P value = 0.02).

Most of our patients had a free distal and proximal surgical margin; radial margin was reported in less than 50 % patients. All of our patients who had any, including radial, involved margin, except for one who had involved distal margin, died. Higher mortality was observed in patients having less than twelve lymph nodes removed as shown in Table 2. There was higher mortality observed for poorly differentiated pathology, mucinous differentiation and signet ring pathology.

Analysis from the patients from our centre suggests that in Pakistani population, patients usually present with advanced stage, there is a male preponderance, relatively mean younger age at presentation for males is found in comparison to females. Advanced stage and lymph node involvement were the two most important factors associated with worse mortality. Pathological features associated with worse prognosis were, poor differentiation, signet ring or mucinous morphology, location in descending colon, positive surgical margins and removal of less than twelve lymph nodes. Most of our findings are in confirmation with the literature from the west. Our analysis underscores and reiterates the importance of adequate early diagnosis and adequate surgery with sufficient lymph node assessment to improve the overall outcome from colon cancer.

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