Original Article

Evaluation of Morphological Prognostic Factors and Survival Rate in Colorectal Cancer Patients

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ABSTRACT

Objective: To evaluate Morphological Prognostic Factors and Survival Rate in Colorectal Cancer Patients of the recent five years.

Study Design: Retrospective cohort study

Place and Duration of Study: This study was conducted at the in Peshawar Institute of Medical Sciences from June 2014 till August 2019.

Materials and Methods: We collect demographic data in the form of age, sex, body mass index, last date of contact, history of consuming betel nut along with the history of smoking to check the association of cancer with these factors. We include primary site, histological type, grade/differentiation, size of treatment, regional lymph nodes as a general characteristic of tumor.

Results: Factors like age greater than 65, high grade of pathological differentiation, distant metastasis were highly associated with a 5-year risk of death among the colorectal cancer patients. Conclusion: Perineural nerve invasion and distant metastasis are considered as important in early detection. Early detection of these parameters will surely increase the survival rate.

Conclusion: There are a lot of prognosis factors that may affect the survival rate among CCR patients. Some independent variables perineural nerve invasion, distant metastasis, age, pathological differentiation grade, obstruction, and regional lymph node metastasis are independent predictors that highly influence the ratio. But some like perineural nerve invasion and distant metastasis are considered as important in early detection. Early detection of these parameters will surely increase the survival rate.

Key Words: Colorectal Cancer, Betal Nut, Smoking, Histopathology

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INTRODUCTION

All around the world colorectal cancer is one of the third-highest cancer types with 17.3% morbidity and an 8.3% mortality rate. Its ratio is quite high among males as compared to females[1].This disorder usually arises from glandular, epithelial cells of the large intestine. It emerges as a result of mutation inside the epithelial cells[2]. The colon is responsible for reabsorbing water, minerals, and nutrients in the chyme. Death cells during the process come out in the form of feces but sometimes abnormal growth of colon cells cause complexities and turn out in form of cancer[3].

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The development of tumors through the traditional pathway where APC and KRAS mutation arises on the left colon takes more than 5-20 years interval[4]. According to the top-down morphological model, APC mutation arises in the upper crypt compartment[5]. On the other hand, BRAF mutations and epigenomic instability (CIMP-high) occur lower crypt compartment in the right corner and triggers the growth of the tumor[6]. In 2007, the World cancer research fund found a significant association of colorectal cancer with obesity, lack of exercise, high consumption of meat, and alcohol[7,8]. Age factor, hereditary mutations, inflammatory bowel disease, abdominal radiation, cystic fibrosis, cholecystectomy, androgen deprivation therapy, and some medications contribute to the emergence and development of the disease[9]. History of neoplasms, Lynch syndrome boosts the growth of colorectal cancer in 2%-4% cases[10].

In early diagnosis, surgery is considered as the best treatment[11]. In contrast in advanced cases where cancer has 25% metastasized at the time of diagnosis, neoadjuvant, cytotoxic therapies with the rapid evolution of drug resistance are a major source of treatment[12].

In Pakistan, less screening availability, costly treatment, and less awareness of malignancy cause severe complications and enhance the morbidity rate. The public set a general view that there is a little chance of recovery among cancer patients. This research aims to explore the morphological prognostic factors in colorectal cancer and analyze the survival ratio of the recent five years.

MATERIALS AND METHODS

This single-center retrospective study was conducted in the Cancer department of Peshawar institute of medical sciences, from the June 2014 till August 2019. This study was conducted to estimate the survival outcomes in the patients who were diagnosed with colorectal cancer. All the data was extracted from the patient's electrical records. For this study, we include patients who were diagnosed with the international classification of disease oncology, 3rd Edition (ICD-O-3) topographical codes of C18.0-C20.9 (excluding C18.1), and morphology codes of 8000-8152, 8154-8231, 8243-8245, 8247-8248, 8250-8576, 8940-8950, and 8980-8981. Patients who were diagnosed with more than one type of cancer, metastasis to the brain, and very limited survival time e.g fewer than 6 months were excluded from the research.

We analyzed our data by categorizing its stages according to the American Joint Committee on Cancer (AJCC) criteria cancer Further we add site-specific factors included CEA, circumferential resection margin (CRM), tumor regression grade, perineural nerve invasion, KRAS mutation, obstruction, and perforation. Survival rate was noted on the behalf of the last date of contact or death (in some cases).

For the statistical analysis, we used SPSS version 23.0 to apply a t-test for the independent group. $P< 0.05$ was set as significant and two-tail tests were applied for all variables[13].

RESULTS

We conducted this research from 2014 to 2019. A total of 869 patients was diagnosed in this period. Out of 869, 454 (52.24%) were male and the rest were from the female group. Mostly the patients were from the 57 to 75 years of age group with a median age of 64 years. A total of 63.75% of patients was diagnosed with colon cancer and one-third of them belong to stage III with a high percentage of adenocarcinoma (91.71%).

Parameters like regional lymph node metastasis, distal organ metastasis, cancer stage, pathological differentiation, histopathologic type, tumor size, CRM, perineural nerve invasion, KRAS mutation, obstruction, and perforation in Table 2 and 3.

Regression model analysis depicts the values of death and describes the probability of survival for 3 to 5 years in Table 4.

Table No.1: Clinical and Demographic characteristics of patients[13].

Variable	Category	Number of patients (%)
Gender	Male	454(52.4)
	Female	415(47.76)
Age	Median (range, y)	64(17–97)
	Mean ± SD, y	63.7±0.45
	≧65 yr old	434(49.94)
	< 65 yr old	435(50.06)
Primary tumor site	Rectum	315(36.25)
	Colon	554(63.75)
Tumor status	T4	170(19.56)
	T3	468(53.86)
	T1/2	231(26.58)
Regional lymph node involvement	Yes	393(45.22)
	No	476(54.78)
Regional lymph node metastasis	N2	185(21.29)
	N1	208(23.94)
	N0	476(54.78)
Stage	Stage IV	138(15.88)
	Stage III	303(34.87)
	Stage II	238(27.39)
	Stage I	190(21.86)
Distant metastasis	Yes	122(14.04)
	No	747(85.96)
Histology type	Signet ring-cell carcinoma	8(0.92)
	Adenocarcinoma	797(91.71)
	Mucinous carcinoma	64(7.36)
Tumor size	< 50mm	528(65.27)
	≧50 mm	281(34.73)
No. of lymph nodes examined	≧12	647(74.45)
	< 12	222(25.55)
CRM	Positive	47(5.45)
	Negative	47(5.45)
CEA	≧5.0 ng/ml	835(96.09)
	< 5.0 ng/ml	34(3.91)
KRAS mutation	Unknown	801(92.17)
	Yes	25(2.88)
	No	43(4.95)
Perineural invasion	Yes	373(45.32)
	No	496(54.68)
BMI	Unknown	109(12.54)
	18.5–24	374(43.04)
	≥24	386(44.42)
Chewing betel nut	Unknown	106(12.20)
	Yes	30(3.45)
	No	733(84.35)
Smoking	Yes	160(18.41)
	No	602(69.28)
Perforation	Yes	16(1.84)
	No	853(98.16)
Obstruction	Yes	357(41.08)
	No	512(58.92)

Table No.2: Pathological findings of parameters[13]

Variable	Category	Wald	HR	95% CI	p-value
Age	≧65 yr old	19.85	1.87	1.42–2.47	< 0.001
	< 65 yr old				
Tumor status	T4	68.61	8.74	5.23–14.60	< 0.001
	T3	25.03	3.54	2.16–5.82	< 0.001
	T1/2				
Regional lymph node involvement	Yes	58.54	3.05	2.29–4.05	< 0.001
	No				
Stage	Stage IV	88.83	18.96	10.28–34.96	< 0.001
	Stage III	27.19	5.01	2.73–9.18	< 0.001
	Stage II	8.14	2.55	1.34–4.86	0.004
	Stage I				
Distant metastasis	Yes	133.49	5.57	4.16–7.45	< 0.001
	No				
Histology Type	Signet ring-cell carcinoma	4.15	2.80	1.04–7.55	0.042
	Adenocarcinoma				
	Mucinous carcinoma	6.96	1.77	1.16–2.71	0.008
Pathological differentiation	High grade	20.25	2.20	1.56–3.10	< 0.001
	Low grade				
Tumor size	< 50mm				
	≧50 mm	8.75	1.53	1.15–2.03	0.003
CRM	Positive	13.29	2.18	1.43–3.31	< 0.001
	Negative				
KRAS mutation	Yes	7.22	3.90	1.45–10.51	0.007
	No				
Perineural invasion	Yes	83.05	4.43	3.22–6.10	< 0.001
	No				
Perforation	Yes	4.58	2.28	1.07–4.84	0.032
	No				
Obstruction	Yes	21	1.87	1.43–2.44	< 0.001
	No				

Table No.3: Univariate regression analysis[13]

Variable	Category	Wald	HR	95% CI	p-value
Age	≧65 yr old	19.85	1.87	1.42–2.47	< 0.001
	< 65 yr old				
Tumor status	T4	68.61	8.74	5.23–14.60	< 0.001
	T3	25.03	3.54	2.16–5.82	< 0.001
	T1/2				
Regional lymph node involvement	Yes	58.54	3.05	2.29–4.05	< 0.001
	No				
Stage	Stage IV	88.83	18.96	10.28–34.96	< 0.001
	Stage III	27.19	5.01	2.73–9.18	< 0.001
	Stage II	8.14	2.55	1.34–4.86	0.004
	Stage I				
Distant metastasis	Yes	133.49	5.57	4.16–7.45	< 0.001
	No				
Histology Type	Signet ring-cell carcinoma	4.15	2.80	1.04–7.55	0.042
	Adenocarcinoma				
	Mucinous carcinoma	6.96	1.77	1.16–2.71	0.008
Pathological differentiation	High grade	20.25	2.20	1.56–3.10	< 0.001
	Low grade				
Tumor size	< 50mm				
	≧50 mm	8.75	1.53	1.15–2.03	0.003

CRM	Positive	13.29	2.18	1.43–3.31	< 0.001
	Negative				
KRAS mutation	Yes	7.22	3.90	1.45–10.51	0.007
	No				
Perineural invasion	Yes	83.05	4.43	3.22–6.10	< 0.001
	No				
Perforation	Yes	4.58	2.28	1.07–4.84	0.032
	No				
Obstruction	Yes	21	1.87	1.43–2.44	< 0.001
	No				

Table No.4: Stepwise cox regression analysis[13]

Variable	Category	Wald	HR	95% CI	p-value
Age	≧65 yr old	32.68	2.36	1.76–3.17	< 0.001
	< 65 yr old				
Regional lymph node metastasis	Yes	11.22	1.81	1.28–2.57	0.001
	No			Ji	
Distant metastasis	Yes	36.48	2.78	2.00–3.87	< 0.001
	No				
Pathological differentiation	High grade	10.54	1.84	1.27–2.66	0.001
	Low grade				
Perineural invasion	Yes	34.26	2.90	2.03–4.14	< 0.001
	No				
Obstruction	Yes	4.94	1.38	1.04–1.84	0.026
	No				

DISCUSSION

In this cohort study, we observed different factors that are correlated with disease and have a huge impact on the survival rate. In this study, we specifically focus on the five-year survival in order to demonstrate the severity of disease in our region. In our selected population expected survival duration mean of I to IV tumor stage lies within 71.27±1.27 with a significant lifestyle nut we didn't find any significant relationship of these with the survival ratio of patients.

In our study, we demonstrate that men had high exposure to CRC as compared to females. This result is in correspondence to many previous studies. The age group with 64 median age was at high risk of CRC. These results are slightly different from the previously conducted study in Taiwan city 2013 where they found high threats among the above 66 year age group[14]. We observed a high five-year survival rate among the patients as compared to the previous study which found only a 55.70% survival rate among the patients of CRC[15]. This differentiation occurs due to the selection of age groups, as they only selected patients above the age of 65 years. By age group, we found the five-yr survival rate was 76.50% in patients younger than 65 and 60.90% in patients ≥ 65 yr old (P<0.001). We found that patients with greater than age 65 were associated with excess hazard for the death of 2.36. The patient's age at the time of diagnosis is an important prognostic factor for all CRC patients[16]. During this time frame, we found 17% of patients age less than 50 years old with a minimum age of 17 years. This ratio predicts that the young population also has a high chance of CRC. We observed that less than 50 years of age group would not be count for screening at the initial stage and have a poor prognosis[17]. We suggest that screening at the initial stage must be initiate among this age group in order to prevent this disorder. Fecal occult blood along with immunochemical methods could easily be implemented in a particular age group. We observed a 68.70 overall five-year survival rate. Our result is far better than the previous results of the health promotion administration of China[17], Fang et al[18], and the American cancer society in which they only found survival rate 63.0%, 55.69%, and 66%, respectively. In our study, we found a 91.20% five-year survival rate for stage I, for stage two 82.20%, for stage III 63.20%, and 21.70% for stage IV. There is an 80%-90% chance of survival with 2.55- 5.01 risk of death among stage I and II patients whereas we found a 68% survival rate along with an 18.96 death rate among stage III and very limited (8%) survival chance with high expectation of death (34.95) among stage IV patients. This result is in accordance with Mathur et al[15] study and higher than some other studies. Some other factors like tumor site, size, grade, histology, lymph node metastasis, perineural nerve invasion along with AJCC T, N, and M independent stage also influence the survival rate of CRC.

Most of the early cases didn't have clear symptoms like muscle infiltration or distant metastases and observed at the time of analysis. These features along with tumor

status, grade level, and regional lymph node influence the survival rate of patients. These results are in the consistency of Yuan et al[19] and Khanjani et al[20] study. Histology type of CRC were the risk factors, we found 1.77 risks of death in signet ring-cell and 2.80 in adenocarcinoma. Total 4.43 ratio of death associated with perineural nerve invasion. Coz regression analysis depicts that perineural nerve invasion helps in the prediction of CRC and this result is in accordance with the previous studies[13-15].

CONCLUSION

There are a lot of prognosis factors that may affect the survival rate among CCR patients. Some independent variables perineural nerve invasion, distant metastasis, age, pathological differentiation grade, obstruction, and regional lymph node metastasis are independent predictors that highly influence the ratio. But some like perineural nerve invasion and distant metastasis are considered as important in early detection. Early detection of these parameters will surely increase the survival rate.

Author's Contribution:

Concept & Design of Study:	Kamran
Drafting:	Mohibullah Khan
Data Analysis:	Ilyas
Revisiting Critically:	Kamran, Mohibullah Khan
Final Approval of version:	Kamran

Conflict of Interest: The study has no conflict of interest to declare by any author.

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