Original article

Prognostic determinants in colorectal adenocarcinoma

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Abstract

Background: Colorectal malignancies are an emerging major cause of morbidity and mortality. The Asian continent has emerged as the next most frequently affected region after western world. In India, colonic cancer is more common than rectal cancer with a male preponderance. The morbidity associated with colorectal malignancies demands better evaluation and study on the prognostic factors associated with it.

Materials and method: The present study was conducted in the Department of Pathology of a tertiary care rural hospital over a period of 05 years (May 2008 to April 2011). Clinically diagnosed patients with colorectal adenocarcinoma underwent resections which were sent for histopathological examination. All the cases were studied in detail with respect to clinical, radiological and pathological findings.

Results and observations: A total of 217 cases of colorectal lesions were received. 98 cases of adenocarcinoma were noted of which 84 cases were of conventional adenocarcinoma, 10 cases of mucinous adenocarcinoma and 4 cases of signet ring adenocarcinoma. 54 (55.10%) cases showed lymphovascular invasion. Follow up period was 6 months to 60 months. At the time of last follow up, 69 patients were alive of which 07 patients were alive with disease (AWD), 56 patients were alive disease free (ADF) whereas 06 patients were lost to follow up. Majority of patients were stage III.

Conclusion: The prognostic determinants of colorectal adenocarcinoma are variable and have strong implications in patient outcome. Higher grade and higher stage have direct relation with worse prognosis.

Introduction

The advent of molecular targeted therapy has dramatically changed the world wide approach to colorectal carcinoma. Asia, in particular India is an emerging hub of gastrointestinal malignancies.[1,2,3]

Patient outcome has a direct relationship with certain determinants such as histopathological diagnosis, subtype, gross morphology and microscopy degree of differentiation presence of lymphovascular and/or perineural invasion and lymph node involvement.[4]

The history of prognosis of colorectal carcinomas dates back in 1930s. Cuthbert Duke's, at St. Mark's Hospital in London devised the first famous prognostic system ie. Duke's staging.[5] For more than 50 years since 1932, Duke's staging of colorectal carcinoma was accepted as the basis of predicting prognosis.[6,7]

In 1949, the modified Duke's staging was introduced which explained in detail the tumor extending through the muscularis propria and those involving the lymph nodes.[8]

In 1954, the well known Astler Coller staging system gained momentum. However, as other drawback of the earlier staging systems, stage A tumors could not be explained in detail in Astler Coller staging system.[9]

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WHO classification of tumors of digestive system 2010, gave the TNM staging of tumors of colon and rectum. This staging system has to a good extent been able to record of clinical and pathological data suggest protocols and for cast the prognosis. The TNM staging takes into account the tumor extent throughout the layers of the bowel, presence and absence of lymph nodes according to regionality and metastasis to one or multiple organs. It is to be noted that each of these parameters are individuals independent prognostic factors.

Other than stage and grade of tumor, aggressive histologic type lymphovascular and perineural invasion, involvement of radial margin and presence of inflammatory cells at the tumor site also are important prognostic determinants in colorectal malignancies.[10]

Aim and objectives: To study in detail the prognostic determinants in colorectal adenocarcinomas.

Materials and method

The present work is a descriptive cross sectional retrospective study done over a period of 05 years from May 2008 to April 2011 in the Department of pathology in a tertiary care rural hospital. All the patients clinically diagnosed as colorectal adenocarcinoma underwent resection. All the specimen were processed by routine standard histopathological processing techniques. The clinical data which included the radiological findings were obtained from the Institutional medical record section and departmental data base of department of Pathology.

Individual cases were studied under, i) age ii) site of tumor iii) location iv) gross morphology v) histological type with subtype vi) grade of tumor vii) extent of tumor viii) presence and absence of inflammatory response ix) lymphovascular invasion x) number, location and extent of lymph nodes involvement xi) presence and absence of metastasis.

TNM staging of colorectal tumors according to the WHO classification of the tumors of colon and rectum was employed to stage the tumors. Follow up was done of all patients for period ranging from 6 month to 60 months.

The data was analyzed and relation between stage, grade and patient outcome was studied.

Observation and results

A total of 217 cases of colorectal lesions were encountered through out 5 year period of which 98 cases were of adenocarcinoma. 84 (85.71%) cases were conventional adenocarcinoma, 10 (10.20%) cases were mucinous adenocarcinoma, 4 (4.08%) cases were signet ring adenocarcinoma.

There were 40 (40.81%) cases of well differentiated and moderately differentiated tumors each with poorly differentiated adenocarcinoma comprising of 18 (18.36%) cases. (Table 1)

Table 1 Distribution of cases according to diagnosis and grade

Diagnosis	Grade of tumor			
	Well	Moderate	Poor	Total
Adenocarcinoma	36	37	11	84
Mucinous adenocarcinoma	04	03	03	10
Signet ring adenocarcinoma	00	00	04	04
Total	40	40	18	98

At the time of last follow up majority of patients were alive with 69 (70.40%) cases of which 07 (7.1%) patients were AWD and 06 (6.1%) patients ADF. 6 patient were lost to follow up and further study could not be done 29 (29.59%) patients died in the course of the diseas ie died of disease (DOD) of the disease. (Table 2)

Table 2 Distribution of cases with respect to outcome

Diagnosis	Outcome			
	AWD	ADF	DOD	LTFU
Adenocarcinoma	05	50	25	04
Mucinous adenocarcinoma	02	05	02	01
Signet ring adenocarcinoma	00	01	02	01

Majority of the patients who were AWD were stage III with 5 cases (5.1%) followed by stage IV with 2 patients. (Table 3) Majority of the patients who were ADF were stage III with 27 (27.55%) cases followed by stage I 22 (22.44%) cases. There were 7 cases who were in stage II.

At the time of last follow up, of the 29 patients who died, majority of patients were in stage IV with 14 (14.28%) cases followed by stage III with 13 (13.26%) cases.

Table 3 Showing relation of stage with outcome

Stage	Outcome		
	AWD	ADF	DOD
I	00	22	02
II	00	07	00
III	05	27	13
IV	02	00	14

The survival rate in grade I and grade II patients was calculated to be 40.81%. were as grade III patients had a low survival rate of 18.36%. Similarly survival rate calculated, revealed stage III patients to have high survival rate that is 34.69% followed by stage I 26.53% with the lowest survival rate 2.04% in stage IV patients.

When compared with the age group affected, prognosis was worst in older ie. more than 50 years age group with a better prognosis in younger patients.

Patients more than 50 years in age were more often seen in stage III and stage IV showing a worse prognosis with increasing age.

Discussion

Prognostication of colorectal malignancies is based on variable dependent as well as independent prognostic factors. The TNM staging system predicts the outcome with fair accuracy. However,

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according to few studies, prediction of outcome in patients with disease in intermediate stage was less accurate as done by TNM staging.[11]

It is to know that 2 patients having same pathologic stage can present with differentiate clinical outcomes.[12,13]

According to WHO classification of colorectal tumors adenocarcinomas has histomorphological variants which individually have a direct relationship with the prognosis.[14] With conventional adenocarcinoma having relatively better prognosis, mucinous adenocarcinoma which contribute about 4-19% of colorectal carcinoma world wide has shown to have a poorer prognosis.[15-21] Signet ring carcinoma on the other hand which is in itself a poorly differentiated adenocarcinoma and characterized by presence of more than 50% of tumor cells with prominent intracytoplasmic mucin, displaced and moulded nuclei have an even more poorer prognosis when compared to the other 2 variants.[22-24]

It is to be noted that signet ring carcinoma there is diffuse involvement of all 4 layers of the bowel ie. linitus plastica.

In our study majority of the tumors were conventional adenocarcinoma of which well as well as moderately differentiated tumor were of equal incidence. However, when compared with poorly differentiated tumors, survival rate in latter cases was low. Poorer the grade, worser is the prognosis. The degree of differentiation is a stage independent factor.[25,26]

Colorectal carcinomas do not spread via the lymphatics as the mucosa lacks lymphatic channels. However, stromal invasion should be evaluated meticulously especially in polypoidal lesions. The T stage characterized by the tumor extent through the bowel wall is an independent prognostic factor which influence survival.[27,28] In T4 stage, meticulous evacuation of the adjacent

structure is of utmost importance. Evaluation of radial margin in cases involving the rectum of histologically diagnosed T3 stage cases cytological examination, serosal scrapping of histologically diagnosed T3 stage cases is extremely important as survival rates are excellent in patients not in stage IV. Hence the need for accurate evaluation.[29,30] The survival rates in stage IV was the least in our study. Tumors extending beyond the submucosa along with those invading the vascular channels predominantly the extramural veins exhibit adverse prognosis.[31] Tumors which exhibit lymphovascular infiltration demand wider excision, so as to prevent possible metastasis or local recurrence.[32,33,34]

Accurate tumor staging is of paramount importance as the treatment protocols are completely different for stage III and stage IV patients. Patients with presence of peritoneal invasion are associated with significant reduction in survival.[35]

Hyperthermic Intraperitoneal chemotherapy (HIPEC) with or without cytoreductive treatment is employed in stage IV tumors. The advent of colonoscopy has bettered the treatment protocols. Introduction of targeted molecular therapies has dramatically changed the outcome of patients.

Conclusion

Colorectal adenocarcinoma is the most common malignancy affecting the colon and the rectum. Tumor stage, degree of differentiation and nodal metastasis are strong individual prognostic factors which help in predicting the prognosis. Better evaluation of these factors can raise the standards of patient management. Judicial application of neoadjuvant therapy is helpful in patients showing variable outcome with similar stage. Further such studies can be under taken in a region wise manner so as to understand better the biological behavior of tumor and help in excellent prognostication and improve standard of life.

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