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Original Article

Retrospective Analysis of Colonic Cancer from a Tertiary Center in South India

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Abstract

Background: Colorectal cancer is the third most common cancer in men (10% of all cancer cases) and the second most common in women (9.4% of all cancer cases) worldwide.

Aim: The objective of this study is to analyze the clinical and pathological pattern and treatment outcome of colon cancer.

Materials and Methods: Retrospective analysis of 102 colon cancer patients treated from January 2014 to January 2016 was analyzed. Age group, sex, stage, performance status, clinical features, and treatment were analyzed.

Results: Colon cancer constitutes 2.45% of total cancer cases seen in our center. More males than females were affected (M:F –1.2:1). Median age at presentation was 54 years. Seventy-one patients (70%) had right-sided colon cancer and ascending colon was the most common site (26%). The remaining 31 patients (30%) had left-sided colon cancer and sigmoid colon was the most common site (25%). Seventy-one patients (70%) presented with abdominal pain, 11 (11%) with altered bowel habits, 18 (18%) with bleeding, and 2 (2%) with obstruction. Adenocarcinoma was the histopathology in all cases and 35 (34%) had Grade 1, 55 (54%) had Grade 2, and 12 (12%) had Grade 3 tumors. Ten patients (10%) presented in Stage I, 29 (28%) in Stage II, 33 (32%) in Stage III, and 30 (29%) in Stage IV.

Conclusion: Colon cancer constitutes 2.45% of all cancer cases seen in this center. More males are affected than females and median age was 54 years. The right-sided colon cancers were more common than left side. Median survival was superior in patients treated with FOLFOX 4 regimen in Stage IV colon cancer.

Key words: 5-fluorouracil and leucovorin, Cisplatin, Colon cancer, FOLFOX 4

INTRODUCTION

According to Indian Council of Medical Research (ICMR) 2014, colorectal cancer (CRC) is the third most common cancer in men (10% of all cancer cases) and the second most common in women (9.4% of all cancer cases). In India, the age-adjusted rate (AAR) for colon cancer is 4.4/100,000 in men and 3.9/100,000 in women and it ranks 8th common cancer among men and 9th among women. The median age at presentation is 55 years.[1] The colon is divided into right and left sides. Tumors of cecum, ascending colon, hepatic flexure, and transverse colon were categorized as right-sided colonic cancers and tumors of splenic flexure, descending colon and sigmoid colon were categorized into left-sided colonic cancers. Classically colon cancer was believed to be a disease of the left or distal colon. Since the 1980s, there has been a persistent trend in the increasing percentage of the right-sided colon cancers with an associated decreasing percentage of the left-sided and sigmoid colon cancers.[2] The management of colon cancer is through multimodality approach. Surgery is the primary modality of treatment. Adjuvant chemotherapy is indicated for patients with Stage II disease high-risk features (obstruction, perforation, lymphovascular invasion, perineural invasion, and margin

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positivity), Stage III. Stage IV patients are treated with surgery followed by palliative chemotherapy and targeted therapy.[3,4] FOLFOX-4 chemotherapy is the standard of care. Cisplatin, 5-fluorouracil (5FU), and leucovorin (LV) can also be given for patients who do not tolerate FOLFOX-4. The 5-year survival rate of the patients with Stage I is 92%, Stage II 63%, Stage III 53%, and Stage IV 11%.

Aim

In this study, we try to analyze the pattern of presentation, clinical features, treatment, and outcome of patients with colon cancer.

MATERIALS AND METHODS

Retrospective analysis of 102 colon cancer patients treated from January 2014 to January 2016 was analyzed. Age group, sex, stage, performance status, clinical features, and treatment were analyzed.

All patients with histopathological documentation of adenocarcinoma of colon were included. Rectosigmoid, rectum, and appendicular cancers were excluded. All patients were staged with AJCC staging system (7th edition). Staging investigations were colonoscopy and computed tomography abdomen and pelvis with contrast.

Chemotherapy includes FOLFOX 4 (Inj. oxaliplatin 85 mg/m² I.V. infusion day 1, Inj. LV 200 mg/m² I.V. infusion days 1 and 2, and Inj. 5 FU 400 mg/m². bolus followed by 600 mg/m² infusion over 3 h. Cycle repeated every 14 days) or Inj. cisplatin 75 mg/m² divided and given over 3 days, Inj. 5 FU 500 mg/m² days 1–3, and Inj. LV 30 mg/m² bolus days 1–3. Cycle was repeated every 21 days for 6 cycles in patients who were not fit for FOLFOX. The other chemotherapy schedules used were weekly 5FU, capecitabine and oxaliplatin (CAPOX), capecitabine, 5FU, and LV because they were not fit for definitive chemotherapy.

RESULTS

Colon cancer constitutes 2.45% of total cancer cases seen in our center. A total of 102 patients with colonic cancer were registered between January 2014 and January 2016. Of these, 54 were male and 48 were female [Table 1]. The M:F ratio is 1.2:1. Median age at presentation is 54 years (range 13–82) [Table 1]; 23 patients (22%) had cancer in cecum, 26 (26%) in ascending colon, 12 (12%) in hepatic flexure, 9 (9%) in transverse colon, 3 (3%) in splenic flexure, 3 (3%) in descending colon, and 26 (25%) in sigmoid colon [Table 2].

Table 1: Patient characteristics

Clinical characteristics	Frequency	Percentage
Age		
Median age	54 years (range 13–82)	
Sex		
Male	54	52.9
Female	48	47.1
M:F	1.2:1	
Dietary history		
Vegetarian	1	1.0
Non-vegetarian	101	99.0
Symptoms		
Abdominal pain	71	69.6
Altered bowel habits	11	10.8
Bleeding	18	17.6
Obstruction	2	2.0
Comorbidities	78	76.5
Type of surgery		
Hemicolectomy	62	60.8
Resection	18	17.6
Colostomy	8	7.8
Histopathologic grade		
Grade 1	35	34.3
Grade 2	55	53.9
Grade 3	12	11.8

Table 2: Tumor site distribution

Tumor site	Number of patients (%)
Cecum	23 (22)
Ascending colon	26 (26)
Hepatic flexure	12 (12)
Transverse colon	9 (9)
Splenic flexure	3 (3)
Descending colon	3 (3)
Sigmoid colon	26 (25)

One hundred and one (99%) were non-vegetarian and 1 (1%) was vegetarian [Table 1]. Seventy-one patients (70%) presented with abdominal pain, 11 (11%) with altered bowel habits, 18 (18%) with bleeding, and 2 (2%) with obstruction [Table 1]. All the patients had histopathology of adenocarcinoma and 35 (34%) had Grade 1, 55 (54%) had Grade 2, and 12 (12%) had Grade 3 tumors [Table 1].

Ten patients (10%) presented in Stage I, 29 (28%) in Stage II, 33 (32%) in Stage III, and 30 (29%) in Stage IV [Table 3]. Majority of the patients (61%) presented with Stage III and Stage IV disease. Seventy-eight (77%) presented with comorbid conditions such as diabetes, hypertension, and coronary artery disease and 24 (23%) had no comorbid conditions [Table 1].

Treatment

Surgery

Sixty-two patients (61%) underwent hemicolectomy, 18 (18%) underwent resection, 8 (7%) underwent colostomy, and 14 (14%) did not undergo any type of surgery due to

poor general condition and/or not willing for treatment [Table 1].

Chemotherapy

Seventy-nine patients (78%) received chemotherapy, 21 (20%) did not receive any chemotherapy due to poor general condition or not willing for chemotherapy, and 2 (2%) were on observation because of Stage I and without any poor risk factors [Table 4].

Among 79 patients, 45 (57%) received FOLFOX 4, 20 (25%) received cisplatin, 5FU, and LV and the remaining 14 (18%) received variable chemotherapy (weekly 5FU, CAPOX, capecitabine, 5FU, and LV) because they were not fit for definitive chemotherapy.

Twelve patients (60%) completed all the planned cycles of cisplatin, 5FU, and LV, 27 patients (60%) completed all the planned cycles of FOLFOX 4 and 4 (29%) completed all planned cycles of CAPOX, 5 FU/LV, capecitabine, and 5 FU/LV. Median survival was 36 months for both FOLFOX4 and cisplatin, 5FU, and LV in Stage I, 36 months versus 35 months in Stage II, 7 months versus 5 months in Stage III, and 6.5 months versus 3 months in Stage IV. Disease-free survival (DFS) at 2 years was 90% in Stage I, 75% in Stage II, 33.3% in Stage III, and progression-free survival was 11.8% in Stage IV. Patients treated with FOLFOX 4 had superior median survival in Stage IV cancers. Sixty-eight patients (86%) defaulted during chemotherapy or during follow-up [Table 5].

DISCUSSION

CRC is the fourth most common cancer in the world. Physical inactivity, obesity, increased alcohol consumption, and long-term smoking attribute to this higher burden. Incidence of colon cancer is significantly lower in India for both genders when compared to that of the West. In India, the AAR for colon cancer in men is 4.4/100,000. The incidence rate in women is 3.9/100,000.[1]

In this study, colon cancer constitutes 2.45% of total cases registered from January 2014 to January 2016. Men are more commonly affected. M:F is 1.2:1. In Western countries, the incidence of colon cancers has decreased overall due to screening of population over the age of 50. However, there has been a dramatic increase in younger patients. A study using data from surveillance epidemiology and end results, found rising incidence in patients aged 20–49 in the past 20 years. In our center, the median age at presentation was 54 years.[5]

Classically colon cancer was believed to be a disease of the left or distal colon. Since the 1980s, there has been a persistent trend in the increasing percentage of the right-sided colon cancers with an associated decreasing percentage of the left-sided and sigmoid colon cancers.[2]

Similar trends have been observed in our center. Seventy-one patients (69.6%) presented with the right-sided colon cancer and ascending colon was the most common site (26%). The remaining 31 patients (30%) had left-sided colon cancer and sigmoid colon was the most common site (26%).

Patients with colon cancer usually present with rectal bleeding, pain, or a change in bowel habits. Occasionally, patients will present with a malignant large bowel obstruction. In our center, the most common presentation was abdominal pain. Only two patients presented with obstruction.

Majority of the patients (61%) were in Stage III and Stage IV. Grade 2 (moderately differentiated) tumors were more common (54%) than Grade 1 (34%) and Grade 3 (12%).

Sixty-two patients underwent hemicolectomy and the remaining either resection or diversion colostomy. Among the 102 patients, 79 patients (77.5%) received chemotherapy.

Table 3: Stage distribution

Stage	Number of patients (%)
Stage I	10 (10)
Stage II	29 (28)
Stage III	33 (32)
Stage IV	30 (30)

Table 4: Chemotherapy details (79 patients)

Chemotherapy regimen	Number received (%)	Stage I	Stage II	Stage III	Stage IV	Number completed chemotherapy (%)	Number defaulted during chemotherapy (%)	Number defaulted during follow-up (%)
FOLFOX 4	45 (57)	3	14	18	10	27 (60)	18 (40)	21 (47)
Cisplatin, 5 FU and LV	20 (25)	2	6	5	7	12 (60)	8 (40)	7 (35)
Others (capecitabine and oxaliplatin, weekly 5FU, capecitabine, 5FU, and LV)	14 (18)	2	2	3	7	4 (29)	10 (71)	4 (29)

Table 5: Survival outcome (at 24 months)

Stage	Disease-free survival (%)	Progression-free survival (%)
I	90	-
II	75	-
III	33.3	-
IV	-	11.8

The evolution of chemotherapy for colon cancer began with the development of 5-FU in 1957.[6] Biochemical studies demonstrated that the main route of 5-FU activation proceeds through complex metabolic pathways that result in the formation of 5-fluorodeoxyuridine monophosphate, a potent inhibitor of thymidylate synthase. The next key advance in the development of 5-FU-based chemotherapy was the finding that inhibition of thymidylate synthase by 5-FU could be potentiated by increased intracellular levels of reduced folates.[7]

Scheithauer *et al*.[8] showed that objective tumor response was 34% in patients treated with cisplatin, 5FU, and LV. The median survival time was 11.5 months (range, 1.5–33.5 months), with 40% of the patients alive at 1 year and 15% at 2 years. In our study, median survival was 36 months for both FOLFOX4 and cisplatin, 5FU, and LV in Stage I, 36 months versus 35 months in Stage II, 7 months versus 5 months in Stage III, and 6.5 months versus 3 months in Stage IV.

The IMPACT study (International Multicenter Pooled Analysis of CRC Trials) pooled data from three randomized trials that investigated high-dose 5-FU/LV compared with no adjuvant therapy. 5-FU/LV reduced mortality by 22% ($P¼ < 029$) and cancer-related events by 35% ($P < 0.0001$) compared with no adjuvant therapy.[9]

In 2004, an interim analysis of data from the pivotal MOSAIC (Multicenter International Study of oxaliplatin/5-FU/LV in the Adjuvant Treatment of Colon Cancer) trial showed that FOLFOX significantly improved 3-year DFS compared with 5-FU/LV (78.2 vs. 72.9%) in patients with Stage III colon cancer.[10]

The final analysis of data from MOSAIC in 2009 confirmed statistically significant improvements in DFS and OS for FOLFOX compared with FL (5-year DFS: 73.3% vs. 67.4%, respectively [$P = 0.003$]).[11] The MOSAIC findings established FOLFOX as the standard adjuvant therapy for resected Stage III colon cancer.

Gustavsson *et al*. presented a historical review of systemic chemotherapy in the adjuvant and metastatic settings, highlighting the key studies that have driven the development of chemotherapy for patients with colon cancer.[12]

A study from Rajasthan shows that in all stages (except Stage IV), FOLFOX-4 protocol yielded above 80% 5-year survival.[13]

In our study, improved median survival at 24 months was noted in patients treated with FOLFOX4 regimen in Stage IV. Sixty-eight patients (86%) defaulted during chemotherapy or during follow-up. This may be due to lack of awareness and family support, belief on native treatment, and poor socioeconomic conditions.

CONCLUSION

Colon cancer constitutes 2.45% of all cancer cases seen in this center. This study of 102 patients with colon cancer shows male predominance. Median age was 54 years. The right-sided colon cancers were more common than left side. Median survival was superior in patients treated with FOLFOX 4 regimen in Stage IV. Due to poor socioeconomic status, lack of family support, and belief on native treatment status, there are a large number of defaulters during treatment and follow-up which affected the treatment outcome.

Limitations

Limitation of this study is that it is retrospective study.

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