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Research Article

Clinico-Pathological Characteristics and Treatment Outcomes of Patients with Stage II Colon Cancer, Single Institutional Experience

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Abstract

Introduction: Colorectal cancer is the third most commonly diagnosed cancer worldwide constituting 10% of total cancer cases, it's the second cause of cancer deaths worldwide. In Egypt colorectal cancer is the ninth most commonly diagnosed cancer. Surgical resection is the only curative treatment for locoregional colon cancer [1]. Adjuvant chemotherapy was found to be beneficial in stage III disease, while in stage II disease its benefit is less certain. We aimed in our work to describe the demographics and clinico-pathological features of patients with stage II colon cancer, whether they received adjuvant chemotherapy or not and the outcome of this population as a part of the NCI experience in the period between January 2013 and December 2018.

Patients and Methods: This retrospective cohort study was conducted at the National Cancer Institute, Cairo University, and included patients diagnosed with stage II colon cancer in the period from January 2013 to December 2018.

Results: A total of 89 patients with stage II colon cancer were included with mean age 50.42 ±13.13 years, 52.8% were below the age of 50, male patients represented 58.4%, right sided tumors were present in 57.1% of patients and 42.9% were in left colon, adjuvant chemotherapy was given to 62.8% of patients, Adjuvant chemotherapy was associated with significant improvement in DFS at 5 years 79.6% vs 62.6% (p 0.036) and OS 92.6% vs 76.4% (p 0.026) compared to surveillance only.

Conclusion: in our study adjuvant chemotherapy was associated with better DFS and OS in patients with stage II colon cancer compared to surveillance only.

Keywords: Colon Cancer; Stage II; Adjuvant; Fluoropyrimidine; Oxaliplatin; High Risk Features; National Cancer Institute

Summary

Colorectal cancer is the third most commonly diagnosed cancer worldwide constituting 10% of total cancer cases, about 1931590 new cases of colon cancer were diagnosed in 2020 worldwide, it's the second cause of cancer deaths worldwide with 935173 estimated deaths from colorectal cancer in 2020 worldwide (about 9.4% of total cancer deaths [1,8]. In Egypt colon cancer is the ninth most commonly diagnosed cancer with 3430 newly diagnosed cases in 2020 constituting 2.5% of total new cases of cancer, and it's the eleventh cause of cancer mortality with 1910 (2.1%) of deaths in 2020. CRC incidence increases with age, but early onset CRC between ages of 40 to 49 incidence has been rising. Risk factors of colorectal cancer include genetic factors as in hereditary CRC syndromes (familial adenomatous polyposis and Lynch syndrome), other risk factors include ulcerative colitis, Crohn's disease, abdominal irradiation, acromegaly, renal transplantation, obesity, diabetes mellitus, red and processed meat, tobacco smoking, alcohol use, the use of androgen deprivation therapy and cholecystectomy [2-5,9]. Colon cancer may present with change in bowel habits, rectal bleeding, iron deficiency anemia and abdomi-

nal pain or symptoms of metastatic disease. Surgical resection is the only curative treatment for locoregional colon cancer. Adjuvant chemotherapy was found to be beneficial in stage III disease, while in stage II disease its benefit is less certain. Adjuvant chemotherapy may be considered for stage II disease when number of analyzed lymph nodes is fewer than 12, in pT4 lesions, if the patient presented with perforation or intestinal obstruction, in poorly differentiated histologies as long as not MSI- unstable, lymphovascular or perineural invasion, mismatch repair enzyme (MMR) status and presence of other comorbidities and anticipated life expectance [6,7]. This retrospective cohort study was conducted at the national cancer institute, Cairo University, a tertiary cancer center, and included patients diagnosed with stage II colon cancer at NCI in the period from January 2013 to December 2018. The study included all pathologically proven stage II colorectal cancer patients (n = 89) who were diagnosed, treated and followed up in the National Cancer Institute in the period from January 2013 till December 2018. The mean age of the studied patients was 50.42 ± 13.13 years (range: 24-78 years), the number of male patients was 52 (58.4%) while the female was 37 (41.6%), Family history of malignancy was reported in 25.8% of cases with 14.6% showing positive family history for colon cancer. Bleeding per rectum was reported in 34.8% of patients, abdominal pain in 56% of patients, change in bowel habits in 42.7% of patients, intestinal obstruction in 16.9% of patients and anemia was reported in 75.5% of patients and only 1.1% presented with abdominal mass. About 57.1% of tumors were in right colon and 42.9% were in left colon. Adenocarcinoma was the predominant histological subtype while adenocarcinoma with mucinous differentiation presented in 3% of cases. Grade II tumors were the dominant grade presenting 84% of cases followed by grade III. About 87.6% of the patients had T3 tumors. Obstruction occurred in 16.9% of the cases while perforation was encountered only in 6.7% of the cases. Preoperative CEA was high in 22.2% of the cases while preoperative CA19.9 was high in 10.9% of them. 87.3% of the patients were anemic at presentation with the mean hemoglobin level was 10.4 ± 1.7 g/dl (range: 7.4-14.4 g/dl). TLC was high in only 15.18%. Adjuvant chemotherapy was given to 56 patients (62.9%) of patients. About 53.6% received less than 6 cycles and 46.4% received more than 6 cycles. About 80.4% received xeloda only and the rest received other types of chemotherapy (RP, XELOX, FLOX, and FOLFOX). Fluoropyrimidine only chemotherapy was given to 47 patients 5FU only, and 9 patients received fluoropyrimidine plus oxaliplatin. The median duration of adjuvant chemotherapy was 4.5 months (ranging from 0.75 to 6 months). Treatment toxicity occurred in 42.8% of the patients and 17.8% showed grade 3 or 4 toxicity. The most common toxicities were hand and foot syndrome (19.6%) followed by diarrhea and peripheral neuropathy in 17.8% and 14.2%, respectively. This study included 89 patients who were followed up for at least 3 months, the median follow up period was 46.6 months. At the end of follow up period, 19 patients showed evidence of disease recurrence or death and 9 were dead. The median OS was not reached with cumulative survival proportion of 91.8% and 86.9% at 3 year and 6 years, respectively. The cumulative 5-year OS was 86.9%. And the median DFS was not reached with cumulative disease free proportion of 82% and 73.6% at 3 year and 6 years, respectively. There was observed better survival in the younger age group with 5 year OS 93.2% vs 80.3% but that was not statistically significant (p = 0.054). Patients who presented with bleeding per rectum had significantly better DFS (p 0.040). Patients with T4 tumors showed a trend toward worse DFS (p value 0.094) but not OS, elevated baseline TLC was associated with improved DFS (P = 0.042), and presence of anemia at diagnosis showed better DFS and OS (p values 0.013 and 0.006 respectively). In Figure 1 and 2, adjuvant chemotherapy was associated with significant improvement in DFS 79.6 vs 62.6 (p 0.036) and OS 92.6 vs 76.4 (p 0.026). Patients who received oxaliplatin plus fluoropyrimidine CTH showed worse DFS compared to patients who received fluoropyrimidine only CTH 38.1% vs 86.1% (p 0.003), the overall survival was similar between the 2 groups 88.9 vs 93.2% (p 0.365).

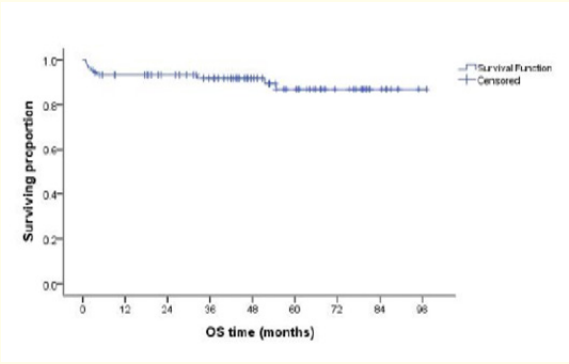

Figure 1

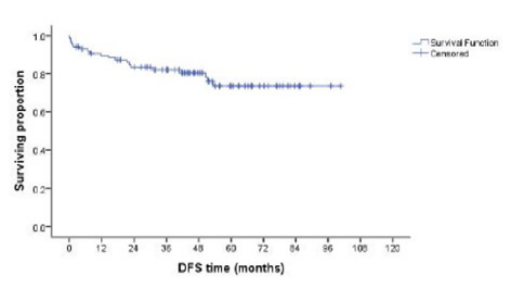

Figure 2

Conclusion

Based on this hospital based retrospective study after assessment of 89 patients with stage II colon cancer, adjuvant chemotherapy was associated with better DFS and OS regardless of high risk features.

Recommendations

- Ensuring that pathology reports be thorough and commenting about if any high risk pathological features are present or not including lymphovascular invasion (LVI) or perineural invasion (PNI) or tumor budding.
- Routine use of microsatellite instability (MSI) testing for patients with stage II colon cancer to help guide the decision of adjuvant CTH.
- Strict follow-up of patients after treatment for early detection of disease recurrence.
- Considering adjuvant chemotherapy for patients with stage II colon cancer especially those with high risk features, MSI stable, or low.

For patients with MSI high, and high risk features considering addition of oxaliplatin to fluoropyrimidine based CTH.

- Larger population based PROSPECTIVE STUDIES ARE needed to confirm the results of our study.
- Larger studies are also needed to assess benefit of circulating tumor DNA (ctDNA) based risk stratification for stage II colon cancer in comparison with clinicopathological features.

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