Outcome of locally advanced rectal cancer patient treated with chemotherapy and radiotherapy, Retrospective Study

Thesis
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Abstract:

Retrospective study of 46 patients with locally advanced rectum treated with neoadjuvant chemoradiation in NEMROCK. Median survival was affected by socioeconomic status, pretreatment and post-treatment CA19.9, response after neoadjuvant and type of surgery. DFS was affected by pretreatment CA19.9, post-treatment CEA, length of segment affected of rectum, mucinous differentiation, and surgical staging, response was affected by socioeconomic status and site from anal verge and post-treatment CEA and type of surgery.

Key words:

Locally advanced, rectum, concurrent, chemoradiation

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AIM OF WORK

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The present work aims studying the outcome of the locally advanced rectal cancer patients present to Kasr Alainy center of clinical oncology and nuclear medicine (NEMROCK) during the period from January 2004 to December 2014 and received neoadjuvant concurrent chemoradiation as regard response, disease free survival and overall survival and different factors affecting them.

Review of Literature

Epidemiology

Colorectal cancer is the fourth most common cancer and second leading cause to death in both females and males. The American Cancer Society (ACS) estimates that 39,220 new cases of rectal cancer will occur in 2016; 23,110 cases of rectal cancer are expected in men and 16,110 in women. For estimates of deaths, the ACS combines colon and rectal cancers; approximately 49,190 deaths from colorectal cancer; 26,020 in men and 23,170 in women, are expected to occur in 2016. (Siegel, et al., 2016).

- **Race**

The incidence of colorectal cancer tends to be higher in Western nations than in Asian and African countries; however, within the United States, minor differences in incidence exist among whites, African Americans, and Asian Americans. Five-year survival rates are lower among blacks (55%) than whites (66%). Among religious denominations, colorectal cancer occurs more frequently in the Jewish population. (Siegel, et al., 2016).

This racial disparity could be decreased with greater education to the black population regarding colorectal cancer prevention and access to treatment, including colonoscopies and polypectomies. (Robbins, et al., 2012).

- **Sex**

The incidence of rectal cancer is slightly higher in males than in females. The overall age-adjusted incidence of rectal cancer in all races was 15 per 100,000 for males and 9.5 per 100,000 for females in 2009-2013. Mortality rates for colorectal cancer were also higher in males (17.34 per 100,000) than in females (12.2 per 100,000) in 2013. (Howlader, et al., 2016).

- **Socioeconomic and educational status**

Socioeconomic status is an important predictor of stage at diagnosis for colorectal, lung, and cervical cancers. The high socioeconomic status group is more likely to present with local stage disease than those from the low socioeconomic status group. (Schwartz, et al., 2003).

Socioeconomic status (SES) affects survival after a cancer diagnosis.Compared to patients with high education, those with shorter education had poorer relative and overall survival (58.7% 5-year relative survival versus 69.1% in rectal cancer). There were also differences in

diagnostic activity with preoperative computer tomography (40% versus 47.3%) and colonoscopy (56.3% versus 62.8%) being more frequent in highly educated groups ($p = 0.001$ and 0.037, respectively). Surgery resulting in colostomy was performed in 26.9% of rectal cancer patients of high education compared to 35.5% of those with low education ($p = 0.005$).(Cavalli-Björkman, et al., 2011).

Survival rates for rectal cancer, by stage

5 years Survival rate for rectal cancer is 66.6% and it is related to stage at diagnosis. 5 years survival rates for localized stage 88.2%, 77% for regional metastases, and 14%for distant metastases.(Howlader, et al., 2016).

Etiology

❖ Non-modifiable risk factors;

Several risk factors are associated with the incidence of colorectal cancer. Those that an individual cannot control include age and hereditary factors. In addition, a substantial number of environmental and lifestyle risk factors may play an important role in the development of colorectal cancer; modifiable risks factors

1- Age:

Incidence and death rates for rectal cancer increase with age.Overall, 90% of new cases and 93% of deaths occur in people 50 andolder. (Lewis, et al., 2016).

The median age at diagnosis for rectal cancer is 63 in men and 65 in women. The incidence rate at age under than 65 years old is 6.8 per 100.000 and 47.7per 100.000 at age of 65 years old or older.(Howlader, et al., 2016).

Eighty-five percent of colorectal cancer survivors (about 1.2 million men and women) are aged 60 years and older, while only 4% (60,610) are aged younger than 50 years. (Millers, et al., 2016).

In 2030, the incidence rates for colon and rectal cancers will increase by 90.0% and 124.2%, respectively, for patients 20 to 34 years and by 27.7% and 46.0%, respectively, for patients 35 to 49 years.(Bailey, et al., 2015).

2- Personal History of adenomatous polyp:

History of adenomatous polyps increases the risk of colorectal cancer. This is especially true if the polyps were large or if there was more than one. Approximately 30 % of colorectal carcinomas develop via the serrated neoplasia pathway characterized by widespread DNA methylation and frequent *BRAF* mutation. Serrated polyps represent a heterogeneous group of polyps which are the precursor lesions to serrated pathway colorectal carcinomas. The histological classification of serrated polyps has evolved over the last two decades to distinguish three separate entities: hyperplastic polyp, sessile serrated adenoma (SSA), and traditional serrated adenoma (TSA). Serrated polyposis syndrome is now widely recognized as conferring a high risk of colorectal carcinoma although its cause remains elusive. (Rosty, et al., 2013).

3- Personal History of Inflammatory Bowel Disease:

IBD ranks among the top three high-risk conditions for CRC, together with the hereditary syndromes of familial adenomatous polyposis (FAP) and hereditary nonpolyposis colorectal cancer (HNPCC). It only accounts for 1–2% of all cases of CRC in the general population.(Itzkowitz, et al., 2004).

The risk increases with the extent and duration of disease. (Bernstein, et al., 2001).

Approximately 5–10% of IBD patients develop colorectal cancer after 20 years and 12–20% after 30 years of disease. (Munkholm, et al.,2003).

The most common forms of inflammatory bowel disease are ulcerative colitis and Crohn's disease.

The overall prevalence of CRC in any ulcerative colitis patient, based on 116 studies, was estimated to be 3.7%. The incidence rate corresponded to cumulative probabilities of 2% by 10 years, 8% by 20 years, and 18% by 30 years. (Eaden, et al., 2001)

Among patients with Crohn's colitis, it is found a relative risk (RR) of 5.6 for CRC. (Munkholm, et al., 2003).

However, there is some evidence that cancer risk in these patients may be lower in recent years due to improved disease management and the use of screening to detect premalignant lesions. (Jess, et al., 2012).

4- Familial adenomatous polyposis (FAP):

An autosomal-dominant colorectal cancer syndrome caused by a germline mutation in the adenomatous polyposis coli (APC) gene, on chromosome 5q21. APC is a tumor suppressor gene, first localized in 1987, and cloned in 1991 following mutation analyses in unrelated families with FAP. (Groden, et al., 1991).

Patients with FAP develop large numbers of benign adenomatous polyps of the colorectal epithelium in early adulthood. Almost invariably, some of these will progress into invasiveness and, ultimately, metastasize. Left untreated, there is a nearly 100% progression to colorectal cancer (CRC) by the age of 35–40 yr. FAP patients will also develop neoplastic lesions at extracolonic sites, for example desmoids, ampullary carcinomas, and hepatoblastomas. (Näthke, et al., 2004).