Correlation of Outcome of Neo adjuvant Concurrent Chemo radiotherapy with Clinico-epidemiological characteristics in locally advanced rectal cancer patients: retrospective study

A Thesis

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By

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✍ *Wafaa Abd Elmonem Elnemrawy*

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List of Abbreviations

Abbr.	Full-term
ACBE	*Air contrast barium enema*
AJCC	*American joint committee on cancer*
APC	*Adenomatous polyposis coli*
APR	*Abdominoperineal resection*
ASCO	*The American society of clinical oncology*
ASR	*Age-standardized rate*
BPR	*Bleeding per rectum*
CA 19-9	*Cancer antigen 19-9*
CAPOX	*Capecitabine & Oxaloplatin*
cCR	*Complete clinical response*
CDC	*Centers for disease control*
CEA	*Carcinoembryonic antigen*
CI	*Confidence interval*
CRC	*Colorectal cancer*
CRM	*Circumferential margin*
CT	*Computed tomography*
DCBE	*Double contrast barium enema*
DFS	*Disease free survival*
dMMR	*Mismatch repair protein*
ECOG	*Eastern Cooperative Oncology Group*
ERUS	*Endo rectal ultra sound*
ESMO	*European society for medical oncology*
FAP	*Familial adenomatous polyposis*
FOBT	*Fecal occult blood test*
FOV	*Field of view*
H&E	*Hematoxylin and eosin*
HNPCC	*Hereditary nonpolyposis colorectal cancer*

IBD ..... *Inflammatory bowel disease*
IHC ..... *Immune histochemical*
IMRT ..... *Intensity modulated radiotherapy*
LAR ..... *Low anterior resection*
LARC ..... *Locally advanced rectal cancer*
LE ..... *Local excision*
LR ..... *Local recurrence*
LVI ..... *Lympho vascular invasion*
MRF ..... *Meso rectal fascia*
MRI ..... *Magnetic resonance imaging*
MSI ..... *Microsatellite instability*
NA ..... *Not applicable or not reached*
NACRT ..... *Neo adjvant concurrent chemo radiotherapy*
NCCN ..... *National comprehensive cancer network*
NCRP ..... *National cancer registry program*
NCRP ..... *National Population-Based Cancer Registry Program*
NOS ..... *Not otherwise*
NSAIDs ..... *Nonsteroidal ant inflammatory drugs.*
OS ..... *Overall survival*
pCR ..... *Pathological complete response*
PET ..... *Positron emission tomography*
PNI ..... *Peri neural invasion*
RSNA ..... *Radiological society of North America*
SEER ..... *Surveillance, epidemiology and end results*
TME ..... *Total mesorectal excision*
TME ..... *Total mesorectal excision*
UICC ..... *International union against cancer*
US ..... *United states*
VC ..... *Virtual colonoscopy*
VMAT ..... *Volumetric modulated arc therapy*

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Abstract

Background: The treatment of (LARC) is subject to continuous change due to better diagnostic tools, radio therapeutic techniques and chemotherapeutic agents. It is clear, that a multimodality approach is the only way to achieve satisfactory local recurrence and survival rates in this type of cancer.Widespread use of neoadjuvant therapy have all contributed to decrease the rate of local recurrence, raise the quality of life and the probability of overall survival.

Aim of the Work: to correlate clinico-epdemiological factors of locally advanced rectal cancer patients with outcomes of neoadjuvant concurrent chemo radiotherapy (NACRT) regarding disease -free survival (DFS) and overall survival (OS).

Patients and Methods: In this retrospective study, data were collected from files of 100 patients with locally advanced rectal cancer patients with cT3-4 or any cT/cN+ disease assessed using colonoscopy, enhanced computed tomography, and or magnetic resonance imaging, between Jan 2010 and December 2016 in oncology department of Ain Shams faculty of medicine and Nasser institute of treatment and research. The patients received long course radiotherapy (45-50.4 Gy/1.8-2 Gy) combined with concurrent chemotherapy. Surgery was done after NACCRT, Which had been abdominoperineal resection (APR), low anterior resection (LAR), exploration. Data were collected retrospectively by reviewing of medical records (hard copy records, pre treatment radiology, radiotherapy documentation, surgical and pathology reports, and follow up clinic records). Ethics committee of Ain Shams faculty of medicine approved the study

Results: This study showed younger age presentation of our population with median age 44yr. The study showed that grades of rectal cancer having statistically difference with DFS and OS with P value 0.009 and hazard ratio 1.919 with 95% CI. Types of surgery (LAR, APR and exploration) had statistically significant difference and impact on DFS and OS with P value 0.044 and hazard ratio 1.646 with 95% CI. y-pathological nodal staging had statistically significant difference on DFS and OS with P value 0.042 and hazard ratio 1.633 with 95% CI. Pathological response that achieved after CCRT having statistically significant difference on DFS and OS with P value 0.048 and hazard ratio 1.323 with 95%CI. These parameters are independent prognostic factors and considered during management of patients with locally advanced rectal cancer.

Conclusion: assessment of LARC patients before selection type of therapy is very important to select whom patient will benefit from NACRT, will gain functional preservation at the time of surgery and increase probability of overall survival.
Key words: Neoadjuvant Concurrent Chemo radiotherapy, Clinico-epidemiological characteristics rectal cancer.

Introduction

Colorectal cancer is the fourth most frequently diagnosed cancer and the second leading cause of cancer death in the United States. In 2018, 43,030 new cases of rectal cancer are estimated in the United States (23, 110 cases in men; 16, 110 cases in women). During the same year, it is estimated that 50,630 people will die from rectal and colon cancer combined ***(Siegel et al., 2018).***

It accounts for over 9% of all cancer incidence and accounts for about 8.5% of all cancer related mortality. Countries with the highest incidence rates include Australia, New Zealand, Canada and the United States. The countries with the lowest risk include China, India, and parts of Africa ***(Tabaries et al., 2015).***

According to the results of the National Population-Based Registry Program of Egypt 2008-2011, these data showed that ASR of 6 and 4.9 per 100, 000 in men and women respectively. The incidence represents 3.2% of all cancers in both sexes. 1070rectal cancer cases suspected within 2020 (568 males and 505 females with male to female ratio (1.1:1) ***(Amal et al., 2014).***

Modifiable risk factors associated with 30–50% of the colorectal cancer risk is attributable to lifestyle factors such

as smoking, high consumption of red and processed meat, obesity, diabetes, and excessive consumption of alcohol ***(Kolligs et al., 2016).***

Screening for rectal cancer is effective in reducing the mortality risk among the screened population. In A cohort CRC screening feasibility study using fecal occult blood testing, showed a reduction in rectal cancer mortality in screened group compared to being unscreened ***(Jan et al., 2014).***

Other screening tests, such as colonoscopy and sigmoidoscopy, have been proposed. According to a recent randomized trial in the United Kingdom, a one -time flexible sigmoidoscopy screening between 55 and 64 years of age reduced colorectal cancer incidence by 33% and mortality by 43% ***(Atkin et al., 2010).***

The main manifestation of rectal cancer are melena, abdominal pain, unexplained iron deficiency anemia and/or a change in bowel habits with positive family history of colorectal cancer and polyps. Full colonoscopy and Pelvic MRI are required for all rectal cancer patients at time of diagnosis. For detection of distant metastasis, CT of the chest is required ***(Kolligs et al., 2016).***

The treatment of locally advanced rectal cancer is subject to continuous change due to better diagnostic tools,

radio therapeutic techniques and chemotherapeutic agents. It is clear, that a multimodality approach is the only way to achieve satisfactory local recurrence and survival rates in this type of cancer ***(Nordlinger et al., 2012).***

Locally advanced rectal cancer (LARC) has often developed postoperative local recurrence. Widespread use of neoadjuvant therapy have all contributed to decrease the rate of local recurrence, raise the quality of life and the probability of overall survival ***(Joshua and Julio, 2015).***

In an effort to reduce further the incidence of margin positivity, local recurrence and improve survival of rectal cancer, preoperative neoadjuvant radiotherapy with or without chemotherapy has been introduced as adjuvant to total mesorectal excision (TME). A number of trials have reported reduced local recurrence rates and a potential survival advantage associated with preoperative radiotherapy ***(Belluco et al., 2011).***

It also needs to judge and consider the balance between the higher recurrence rate and the higher sphincter-preserving rate. In addition, the evaluation of the efficacy of neoadjuvant radio chemotherapy should be as enough as possible. It needs to maximally improve the accuracy of evaluation ***(Benson et al., 2015).***