RETROSPECTIVE ANALYSIS OF EPIDEMIOLOGY, PROGNOSTIC FACTORS AND RESPONSE OF TREATMENT OF RECTAL CANCER

Thesis

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List of Contents

Title	Page No.
List of Tables	5
List of Figures	7
List of Abbreviations	10
Introduction	1
Aim of the Work	18
Review of Literature	19
Epidemiology	19
Risk Factors	25
Genetic and Molecular Biology	31
Screening	37
Clinical Presentation	40
Pathology	47
Staging & Prognostic Factors	51
Treatment	60
Patients and Methods	68
Results	72
Discussion	106
Summary & Conclusion	115
References	118
Arabic Summary	

List of Tables

Table No.	Title	Page No.

Table (1): Colorectal cancer TNM staging AJCC UICC 8th edition 53

Table (2): Modified Ryan scheme for tumor regression scoring in rectal cancer treated preoperatively..... 55

Table (3): Patients characteristics..... 72

Table (4): Tumor characteristics..... 76

Table (5): Treatment modality 80

Table (6): Pathological findings 83

Table (7): Response to neo-adjuvant CCRTH. 86

Table (8): Median Overall survival (OS) of all patients (60 Cases) 87

Table (9): Disease free survival (DFS) for patients with loco-regional disease with total 49 Cases. 88

Table (10): Progression free survival (PFS) for patients with advanced tumor from the start with total 11 cases. 89

Table (11): Patients characteristics affecting DFS in univariate analysis..... 100

Table (12): Tumor characteristics affecting DFS in univariate analysis..... 100

Table (13): Treatment modalities affecting DFS in univariate analysis..... 101

Table (15): Response of treatment affecting DFS in univariate analysis..... 101

List of Tables (Cont. .).

Table No.	Title	Page No.
Table (14):	Pathological findings affecting DFS in univariate analysis	102
Table (16):	Patients characteristics affecting OS in univariate analysis	103
Table (17):	Tumor characteristics affecting OS in univariate analysis	103
Table (18):	Treatment modalities affecting OS in univariate analysis	104
Table (20):	Response of treatment affecting OS in univariate analysis	104
Table (19):	Pathological findings affecting OS in univariate analysis	105

List of Figures

Fig. No.	Title	Page No.
Figure (1):	Number of new cases of cancer in 2018, all types, both sexes	20
Figure (2):	Afocus of signet ring carcinoma arising within an adenomatous polyp with Left panel of low power view & right panel of higher power view demonstrating typical signet ring cells, which are identified by black arrows	49
Figure (3):	Prognostic impact of the number of positive nodes, total number of nodes examined, and depth of the primary tumor for patients in a population-based cohort of 144,744 patients with colon cancer	59
Figure (4):	Age distribution among studied patients	73
Figure (5):	Gender distribution among studied patients	73
Figure (6):	Patients distributions according to their ECOG performance status	74
Figure (7):	Patients presenting symptoms at the time of diagnosis in all study population	75
Figure (8):	Tumor marker (CEA) assessment pre-operatively among all study population	77
Figure (9):	Tumor site among all study population	77
Figure (10):	Histopathological types among all study population	78
Figure (11):	Clinical T staging classification among all study population.	78
Figure (12):	Clinical N staging classification among all study population.	79
Figure (13):	M staging classification among all study population.	79
Figure (14):	Treatment algorithm	80

List of Figures (Cont...)

Fig. No.	Title	Page No.
Figure (15):	Neoadjuvant CCRT among all study population.	81
Figure (16):	Surgical intervention among all study population.	82
Figure (17):	Pathological staging among all study population	84
Figure (18):	Tumor grading among study population.	85
Figure (19):	Response to neo-adjuvant CCRTH.	86
Figure (20):	Overall survival of all studied population	87
Figure (21):	Disease free survival of all studied population	88
Figure (22):	Progression free survival curve of all studied population	89
Figure (23):	Overall survival according to gender.	90
Figure (24):	DFS according to ECOG PS.	91
Figure (25):	OS according to ECOG PS.	91
Figure (26):	DFS according to presenting symptoms.	91
Figure (27):	OS according to presenting symptoms.	91
Figure (28):	OS according to tumor sites.	92
Figure (29):	DFS according to tumor sites.	92
Figure (30):	DFS according to histopathological type.	92
Figure (31):	OS according to histopathological type	92
Figure (32):	OS according to cT staging.	93
Figure (33):	DFS according to cT staging.	93
Figure (34):	OS according clinical N stage.	93
Figure (35):	DFS according clinical N stage.	93
Figure (36):	DFS according to response to neoadjuvant treatment	94
Figure (37):	OS according to response to neoadjuvant treatment	94
Figure (38):	OS according to pathological T stage.	95
Figure (39):	DFS according to pathological T stage.	95
Figure (40):	Overall survival according to pN stage.	96

List of Figures (Cont...)

Fig. No.	Title	Page No.
Figure (41):	Disease free survival according to pN stage.	96
Figure (42):	OS outcome according to pathological stage.	96
Figure (43):	DFS according to pathological stages.	96
Figure (44):	OS according to tumor grade	97
Figure (45):	DFS according to tumor grade	97
Figure (46):	OS according to CRM status.	97
Figure (47):	DFS according to CRM status.	97
Figure (48):	OS according to status of LVSI.	98
Figure (49):	DFS according to status of LVSI.	98
Figure (50):	OS according to the status of ECE.	98
Figure (51):	DFS according to the status of ECE	98
Figure (52):	OS according to the status of PNI.	99
Figure (53):	DFS according to the status of PNI.	99

List of Abbreviations

Abb.	Full term

ACS ..... *American Cancer Society*

AJCC / UICC ..... *American Joint Committee on Cancer / Union for International Cancer Control*

ALP ..... *Alkaline phosphatase*

APC ..... *Adenomatous polyposis gene*

APR..... *Abdominoperineal resection*

ASCO ..... *American Society of Clinical Oncology*

ASR ..... *Age standardized risk*

CEA ..... *Carcino-embryonic antigen*

CIMP ..... *CpG island methylator pathway*

CIN ..... *Chromosomal instability*

CpG ..... *Cytosine- phosphate- Guanine*

CR ..... *Complete Response*

CRC ..... *Colorectal cancer*

CRCs ..... *Colorectal cancers*

CRM ..... *Circumferential resection margin*

CTC ..... *Computed tomographic colonography*

DCBE ..... *Double-contrast barium enema*

DFS ..... *Disease free survival*

ECE ..... *Extracapsular nodal extension*

EGFR ..... *Epidermal growth factor receptor*

ESD ..... *Endoscopic submucosal dissection*

ESMO ..... *European Society for Medical Oncology*

EUS ..... *Endoscopic Ultrasound*

List of Abbreviations (Cont...)

Abb.	Full term
FAP	*Familial adenomatous polyposis*
FOBTs	*Fecal occult blood tests*
FU	*Fluorouracil*
GI	*Gastrointestinal*
HNPCC	*Hereditary nonpolyposis colorectal cancer*
HR	*Hazard ratio*
IGF-1	*Insulin-like growth factor 1*
IGFBP-3	*IGF binding protein-3*
LAR	*Lower anterior resection*
LCCRT	*Long-course chemoradiotherapy*
LE	*Local excision*
LS	*Lynch syndrome*
LVI	*Lymphovascular invasion*
MAP	*MUTYH-associated polyposis*
MCRC	*Metastatic Colorectal Cancer*
mCRC	*Metastatic colorectal cancer*
MMR	*Mismatch repair*
MRI	*Magnetic Resonance Imaging*
MSI	*Microsatellite instability*
N stage	*Nodal stage*
OS	*Overall survival*
PD	*Progressive Disease*
PET	*Positron emission tomography*
PFS	*Progression free survival*

List of Abbreviations (Cont...)

Abb.	Full term
PNI	*Perineural invasion*
PR	*Partial Response*
PS	*Performance status*
RR	*Relative risk*
SCRT	*Short-course radiotherapy*
SD	*Stable Disease*
SEER	*Surveillance, Epidemiology, and End Results*
TME	*Total mesorectal excision*
TNM	*Tumor, node, metastasis*
TRUS	*Trans Rectal Ultrasound*
TSGs	*Tumor-suppressor genes*
WBC	*White blood cell*
WHO	*World Health Organization*

INTRODUCTION

Colorectal cancer is the third most frequently diagnosed malignancy just behind lung and breast cancer, accounting for about 1.8 million cases each year, and the second cancer causing death worldwide, accounting to more than 850,000 death per year ***(GLOBOCAN, 2018).*** The magnitude of the rectal cancer problem is significant with 40,000 new cases of rectal cancer seen yearly in the United States ***(Jemal et al., 2009).*** An estimated 80,000 new cases in EU countries per year, rectal carcinoma is one of the most prevalent tumor types ***(Smith et al., 2010).***

The 5- and 10-year relative survival rates for people with colorectal cancer are 65% and 58% respectively. When colorectal cancer is detected at a localized stage the 5-year survival is 90% however only *40%* of colorectal cancers are diagnosed at this early stage due to the underuse of screening. If the cancer has spread regionally to involve nearby organs or lymph nodes by the time of diagnosis the 5-year survival drops to 71%. If the disease has spread to distant organs the 5-year survival is 13% ***(American Cancer Society, 2015).***

The risk of CRC increases with age. Median age at diagnosis is about 70 years or slightly older in most European countries ***(Glimelius et al., 2013).***

Incidence of rectal carcinoma is strongly connected with age because ninety percent of cases are diagnosed over the age of 50. It is known that as many as 30 to 50% of individuals older than 50 harbor one or more adenomatous polyps ***(Smith et al., 2010).***

The importance of the timely diagnosis of younger patients with rectal cancer is demonstrated by several studies examining outcomes in these patients. Younger patients tend to present with more advanced disease, and their overall survival has been reported to be inferior to that of older patients ***(Meyer et al., 2010).***

CRC which are distal to the recto-sigmoid junction are designated as rectal cancer. In one-third of the cases, CRC is diagnosed in the rectum, and rectal involvement has a worse prognosis due to a higher rate of local recurrence and a higher incidence of metastasis at diagnosis. Any tumor whose distal margin is seen approximately 15 cm or less from the anal verge by using a rigid proctoscope should typically be classified as a rectal cancer ***(Sagar et al., 2006).***

Regular use of NSAIDs is associated with reduced incidence. Diabetes type II increases the risk and there is probably a causal role of hyperinsulinaemia and insulin-like growth factors. It is well recognized that individuals with inflammatory bowel disease (ulcerative colitis and Crohn's

disease) are at an increased risk for colorectal cancer ***(Beaugerie et al., 2013).***

The literature on risk factors for colorectal cancer is extensive. Diet and dietary components are important, although the risk increases are not marked and not universally seen. Dietary fiber most likely decreases the risk, whereas excessive consumption of red or processed meat most likely increases it. Smoking increases the risk as does at least moderate and heavy alcohol use. It has been noted that an otherwise healthy lifestyle can substantially reduce the risk ***(Kirkegaard et al., 2010).***

Approximately 20% of cases of colorectal cancer are associated with familial clustering. Genetic susceptibility of colorectal cancer includes well-defined inherited syndromes such as lynch syndrome (also known as hereditary non polyposis colorectal cancer [HNPCC]). Therefore, it is recommended that all patients with colorectal cancer be queried regarding their family history and considered for risk assessment ***(Hemminki et al., 2004).***

Screening has the potential to prevent colorectal cancer because it can detect precancerous growths, called polyps, in the colon and rectum. Although most polyps will not become cancerous, removing them can prevent cancer from occurring. Furthermore, regular screening increases the likelihood that colorectal cancers that do develop will be detected at an early