بسم الله الرحمن الرحيم

MONA MAGHRABY

شبكة المعلومات الجامعية

التوثيق الالكتروني والميكروفيلم

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شبكة المعلومات الجامعية

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جامعة عين شمس

التوثيق الإلكتروني والميكروفيلم

قسم

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Retrospective study about the impact of the negative lymph node count on the survival rate of stage III colon cancer

Thesis

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List of Abbreviations

APC : Adenomatous polyposis coli

CIMP : CpG island methylator phenotype

CIN : Chromosomal instability

CK : Cytokeratin

CpG islands : Cytosine and guanine dinucleotides

CRC : Colorectal cancer

CT : Computed tomography

DALMs : Dysplasia-associated lesions or masses

DFS : Disease-free survival

EGFR : Epidermal growth factor receptor

ER-β : Estrogen receptor beta

FITs : Fecal immunochemical tests

IGF : Like growth factor

MRI : Magnetic resonance imaging

NLN : Number of negative lymph nodes

NLNs : Number of negative lymph nodes

NO : Nitric oxide

OS : Overall survival

ROC : Receiver operating characteristic

SEER : Epidemiology, and End Results

TNM : Tumor, Node, Metastases

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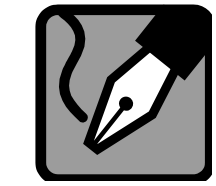

Introduction

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Colorectal cancer is the fourth most frequently diagnosed cancer and the second leading cause of cancer death in the United States. In 2019, an estimated 101,420 new cases of colon cancer and approximately 44,180 cases of rectal cancer occur. During the same year, an estimated 51,020 people will die of colon and rectal cancer combined (**Siegel et al., 2019**).

Despite these high numbers, the incidence of colon and rectal cancers per 100.000 people decreased from 60.5 in 1976 to 46.4 in 2005 **(Cheng et al., 2011**). In fact, the incidence of colorectal cancer decreased at a rate of 3% per year between 2011 and 2015 (**Siegel et al., 2019**). The mortality from colorectal cancer decreased by almost 35 % from 1990 to 2007 **(Siegel et al., 2011)** and is currently down by more than 50% from peak mortality rates (**Siegel et al., 2019**).

These improvements in incidence of and mortality from colorectal cancer are thought to be a result of cancer prevention and earlier diagnosis through screening and better treatment modalities. Despite the observed improvement in the overall colorectal cancer incidence

rate, a retrospective cohort study of the epidemiology, and end results (SEER) colorectal cancer registry found that the incidence of colorectal cancer in patients younger than 50 has been increasing **(Bailey et al., 2014).**

The risk of developing colon cancer depends on factors which can be classified into lifestyle or behavioral factors (such as smoking, high red meat consumption, obesity, physical inactivity) and genetically determinant factors **(Schmoll et al., 2012).**

According to international guidelines, screening tests are stratified according to the personal risk of disease. Age is considered the major unchangeable risk factor for sporadic colon cancer: nearly 70% of patients with colon cancer are over 65 years of age, and this disease is rare before 40 years even if data from SEER and Western registries shows an increased incidence in the 40–44 years group and a decrease in the oldest groups **(Davis et al., 2011).**

Individuals with a personal history of adenoma, colon cancer, inflammatory bowel disease (Crohn's disease and ulcerative colitis), significant family history of CRC or polyps, an inherited syndrome (5–10% of all colon cancers) such as Familial Adenomatous Polyposis coli and

its variants (1%), Lynch-associated syndromes [hereditary non polyposis colon cancer (3–5%)], Turcot, Peutz-Jeghers and MUTYH-associated polyposis syndromes, are considered at high risk of colon cancer and must be actively screened and, in cases of inherited syndromes, also referred for genetic counseling **(Schmoll et al., 2012 & Balmaña et al., 2013)**.

The prognosis of colon cancer is clearly related to the staging features of the TNM classification, including the degree of penetration of the tumor through the bowel wall and the presence, or absence, of nodal involvement. However, many additional parameters such as grading, lymphatic or venous or perineural invasion, lymphoid inflammatory response and involvement of resection margins, which are reflected by the Dukes and TNM classifications, have been shown to have strong prognostic impact **(Amin et al., 2017).**

Lymph node metastasis is regarded as an indubitable prognostic factor for predicting disease recurrence and survival in patients with colorectal cancer. Lymph node status based on examination of a resected specimen is a key element of the current staging system and is also a crucial factor to determine use of adjuvant chemotherapy after

surgical resection. Analysis of data showed that increased number of lymph nodes examined was associated with increased survival for patients with both node-negative and node-positive disease **(Le Voyer et al., 2003)**.

In addition, results from population-based studies show an improvement in survival and examination of greater than or equal to 12 lymph nodes **(Lykee et al., 2013)** However, the current tumor-node-metastasis (TNM) staging system only incorporates the number of metastatic lymph nodes in the N category. Numerous attempts have been made to supplement this simplified N staging including negative lymph node number, lymph node ratio, distribution of metastatic lymph nodes, tumor deposits, or extracapsular invasion. In addition, several attempts have been made to identify more specific prognostic factors in resected colorectal specimens than lymph node status **(Hye et al., 2019).**

Some studies have identified the number of negative lymph nodes (NLNs) that is defined as regional nodes examined minus regional nodes positive as positively related to survival, but the findings have been inconsistent, and the underlying mechanisms have not been clarified **(Degiuli et al., 2018).**