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Prognostic factors for colorectal cancer survival and relapse

Factores pronósticos de supervivencia y recurrencia en cáncer colorrectal

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ABSTRACT

Colorectal cancer is an entity that has been gaining greater epidemiological importance in Latin America on a daily basis. Multiple factors have been described that help predict the prognosis of patients and determine their treatment.

Keywords: Colorectal carcinoma; Microsatellite instability; Histopathology; Prognostic factors.

RESUMEN

El cáncer colorrectal es una entidad que cada día cobra una mayor importancia epidemiológica en América Latina, se han descrito múltiples factores que ayudan a predecir el pronostico de los pacientes y a determinar el tratamiento de los mismos.

Palabras clave: Carcinoma colorrectal; Inestabilidad microsatelital; Histopatología; Factores pronósticos.

To the Editor:

After meticulously reading and making a critical review of the article "Surgical treatment of colon cancer at Central Military Hospital of the Armed Forces in Asunción, Paraguay from February 2017 through February 2019," the fact that the rate of neoplastic colon lesions has increased lately at the doctor's office—both in outpatient care and emergency services—is undisputed. Currently, the use of diagnostic methods make it possible to determine the stage of the disease in terms of local compromise or spread to other structures, which helps establish oncologic management plans based on surgery associated with adjuvant and neoadjuvant therapy that extends the disease-free interval, and eventually the patient's survival.[1] Although the authors mention the presence of novel diagnostic aids and prognostic factors, they did not include them in their study despite the fact that they have a considerable number of patients. The analysis of these data would have been interesting if we think that colorectal cancer (CRC) is the fourth leading cause of death associated with cancer worldwide with a significant prevalence in male patients regarding mortality and incidence rate. Epidemiologically, around 77/1000 patients die every year for this reason worldwide. In Colombia, it is the third leading cause of death due to cancer followed by prostate and lung carcinomas.[2]

Among the main prognostic factors that can be assessed through the existing new technologies to determine risk of disease relapse and overall survival of patients, the following stand out: Histological findings: Compromise of resection borders, compromise of radial border (mainly in rectum cancer), high mitotic activity, high histological degree, signet-ring cell morphology, lymphovascular and/or perineural invasion, macroscopic tumor perforation, tumor implants into the abdominal cavity; all these intrinsic factors of the lesion determine a more unfavorable prognosis in patients who have them.[3]

Intratumor lymphocyte inflammatory Infiltrate: the presence of a high tumor infiltrating lymphocyte (TILs) count is established as a positive prognostic factor in many malignant neoplasms including colorectal carcinoma. In 2014, the TIL International Work Group (ITWG) proposed a standardized methodology to evaluate TIL early in the context of breast cancer. The ITWG system to assess the density of stromal TIL is categorized into 3 groups based on their count: low (0% to 10%), intermediate (15% to 50%), and high (55% to 100%). Survival increases with higher lymphocyte count; with a mean of 53, 67, and 75 months, respectively in each subgroup.[4] Mutation of the KRAS/NRAS: the RAS signaling pathway, also called the chromosomal instability pathway, shows deregulation in, at least, one gene in over 70% of colorectal carcinomas, Kras-activating mutations were found in 30% to 40% associated with a deficient response to anti-EGFR therapies in primary or metastatic disease. The state of the KRAS/NRAS mutation modifies the management of the patients, the updated clinical practice guidelines of the National Comprehensive Cancer Network (NCCN) in oncology recommend that the tumors of all the patients with stage IV disease should be analyzed to detect the KRAS gene and only patients whose tumors have normal Kras (wild type) should receive cetuximab and panitumumab.[5]

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Microsatellite instability: it is significant that in patients with colorectal cancer the hereditary component and the association with genic repair defects known as microsatellite instability are accompanied with a greater predisposition to develop colorectal carcinoma, and extracolonic ones due to mutations in genes MLH1, MSH2, MSH6, and PMS2. The study of instability is conducted through immune-histochemistry and PCR; the most common mutations are those of MSH2 and MLH1 with rates of 40% to 60%, and 40% to 50%, respectively. The other two genes have smaller rates given by MSH6 (10-20%) and PMS2 (2%). Approximately 80% of the CRC with instability are due to hypermethylation of MLH1 while 20% is associated with germinal mutations of MMR genes (mismatched repair).[6]

Patients with microsatellite instability have proven to have better prognosis as opposed to those who don't, above all, thanks to the therapy targeting the PD-1 receptor (nivolumab, pembrolizumab) with good rates of residual disease-free time 12 months after treatment. However, in patients who show loss of some of the microsatellites, BRAF mutations should be studied because these patients are going to have a lower therapeutic response to treatment therapies aimed at the epidermal growth receptor (EGFR).[7]

Considering the above, the analysis of these variables in patients suffering from colorectal cancer could predict their prognosis, as well as guide the treatment and actions to follow as part of a comprehensive approach. Local studies are necessary where these factors are evaluated to determine the behavior of this entity in our environment and establish healthcare strategies to overcome this disease that is gaining greater epidemiological significance by the hour. Therefore, we suggest including these variables in upcoming studies.

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