## CURRENT ISSUES ON THE UNDERSTANDING OF LOCALLY ADVANCED COLORECTAL CANCER

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HEADINGS - Colorectal neoplasms, surgery.

Radical surgery is still the mainstay of management of colorectal cancer<sup>(3,5)</sup> Even though multimodality approach has a definitive place, particularly in the management of rectal cancer, proper "radical" surgery is the only chance for cure for most of patients with this disease<sup>(4)</sup>.

In the current issue of ARQUIVOS de GASTROENTEROLOGIA, a very interesting study on prognostic factors after radical surgery for locally advanced colorectal cancer by Campos et al. (2), brings up a series of aspects relevant to the current literature that deserve consideration.

First of all, the definition of what is a "locally advanced colorectal cancer" has not been standardized. Not even classification systems, such as the AJCC TNM<sup>(1)</sup> staging classification, created to assist in the planning and assessment of treatment results and to allow proper exchange of information between different centers has formally defined such term. Even though the term has been frequently used as a synonym for tumors invading adjacent structures, and therefore deeming sole resection of the colon or rectum insufficient, this definition may lead to rather significant imprecision. Perhaps an interesting alternative definition would be of a cancer that can not be resected without a high likelihood of leaving microscopic or gross residual disease at the local site because of tumor adherence or fixation.

In addition, when analyzing the results of any treatment, one needs to know the exact or at least estimated denominator of a given patient population. In any patient population with "locally advanced colorectal cancer", there will be a proportion of patients that will harbor unresectable disease that will never undergo radical surgery for surgical or oncological reasons. Inclusion of such patients in the denominator is of paramount importance for the estimation of the true incidence of this "locally advanced" condition.

However, there is no question that the oncological outcomes after surgical resection of these tumors is the most relevant information provided by any study concerning such "locally advanced" condition. Again, by excluding unresectable cases, one is examining the results of a highly selected subset of patients instead of the results of surgical management of locally advanced colorectal cancer. One could argue that grouping of patients with rectal and colon cancer together could have been inappropriate, particularly when the

study indicated worse results among rectal cancer patients. Also, grouping of patients with and without neoadjuvant chemo radiation may have contributed to another significant source of bias. However, the considerably small numbers of each of these subsets of patients correctly prompted authors to do so for statistical reasons. With all these inherent limitations in mind, the search for prognostic factors is definitively relevant and increases significantly the interest in this study. Inclusion of clinical, surgical and pathological data capable of affecting survival suggested the role of several factors potentially implicated in oncological outcomes of these patients. Of note is the absence of influence of actual neoplastic adjacent organ invasion when compared to inflammatory adhesions in the study reported by Campos et al. (2). The most recent edition of the AJCC TNM classification system suggests subdivision T4 colorectal cancer that should definitively be considered in future studies. In this 7th edition, the authors distinguish T4 colorectal cancer into T4a whenever the tumor invades directly into the visceral peritoneum and T4b whenever an adjacent organ is actually invaded<sup>(1)</sup>. The review of a significantly large database suggested that these tumors may behave differently and are independent prognostic factors.

The issue of management of colorectal cancers invading adjacent structures is highly relevant and far from being resolved. The exclusion of patients that harbor unresectable disease and never undergo primary resection should not underestimate the incidence of this highly complex condition. Studies should definitively search for prognostic factors among these patients, including recognized staging classification features, allowing for proper comparison between experiences and institutions. Not only these prognostic factors should be controlled for possible confounding variables (independent prognostic factors) but also aimed for specific outcomes including local recurrence, disease-free and overall survival. Understanding of the influence of each of the factors on each of the outcomes may perhaps allow improved and more substantiated management of these patients.

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