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Editorial

Value of Tumour Resection in Colorectal Cancer With Unresectable Metastases[☆]

Valor de la resección tumoral en el cáncer colorrectal con metástasis irresecables

In spite of the lack of scientific evidence, the resection of primary tumors in asymptomatic patients with colorectal cancer (CRC) with unresectable synchronous metastases was a common practice in many centers until the mid-1990s. This method was able to control any possible complications derived from the primary tumor, which occurred in about 20% of patients.¹ Nonetheless, after the implementation of new chemotherapy drugs and the improvement in overall survival of patients with stage IV CRC, current publications, as well as the American Society of Clinical Oncology (ASCO), advocate chemotherapy as initial treatment for these patients, reserving surgery for patients with symptoms derived from the primary tumor or with risk of intestinal obstruction.²

This change in treatment strategy is based on the fact that chemotherapy has beneficial effects not only on metastatic disease but also on the primary tumor.³ In this way, the number of complications related with the primary tumor has been seen to decrease to about 7%.⁴ The effect of chemotherapy on survival becomes apparent when we compare the periods of treatment when only fluoropyrimidines were used with current treatment regimes, after the implementation of modern chemotherapy drugs (oxaliplatin or irinotecan) and biological agents (bevacizumab, cetuximab).⁵⁻⁷

Some recent studies conclude that the resection of the primary tumor before administering systemic chemotherapy in patients with CRC, unresectable metastases and good performance status improves the prognosis in these patients.^{8,9} At the same time, other groups argue that the benefits of initial primary tumor resection on survival have not been demonstrated; in addition, the morbidity and mortality of surgery should be avoided, especially since this could delay the start of chemotherapy and its potential benefits on survival.^{4,10-12}

Different studies observe a longer mean survival in patients with resection of the primary tumor compared to those who are not resected.^{8,9,13,14} These are retrospective, non-randomized studies, which could mean that the patients who were treated surgically presented a better performance status or had a lower tumor load. Greater toxicity to chemotherapy has also been observed in patients without resection when compared to a group of patients with resection of the primary tumor.

Recently, the Dutch Colorectal Cancer Group published a study¹⁴ that evaluated the prognostic value of primary tumor resection depending on the first line of treatment received according to the CAIRO and CAIRO2 studies.^{15,16} The results showed a mean survival of 13 months in the non-resection group versus 22-24 months in the resection group. Despite the difference observed, the patients were not randomized before the tumor resection, which could mean that the characteristics of the patients were not homogeneous. Our group has observed that the 2-year survival in patients with intestinal obstruction due to unresectable stage IV colorectal cancer who had tumor resection is greater than in the patients without tumor resection (39.3% versus 1%, respectively).¹⁷

Other workgroups have tried to resolve this dilemma by formulating different questions. Such is the case of The National Surgical Adjuvant Breast and Bowel Project C-10 (NASBP C-10) group, which specifically asked if the addition of bevacizumab to FOLFOX increases the number of complications in patients with stage IV CRC without resection of the primary tumor.¹⁸ The results showed that only 14% of patients presented major complications (obstruction, perforation, or hemorrhage), so the authors concluded that the incidence of severe complications was acceptable when the primary lesion was not resected. In addition, they emphasized that the

[☆] Please cite this article as: Biondo S, Frago R. Valor de la resección tumoral en el cáncer colorrectal con metástasis irresecables. Cir Esp. 2013;91:349-351.

survival was not compromised by leaving the primary tumor *in situ*.

More recently, the University College Hospital in London initiated a clinical trial with the main objective to determine whether overall survival in patients with stage IV asymptomatic CRC with unresectable metastasis is greater in patients treated with chemotherapy alone or with resection of the primary tumor plus chemotherapy, as described at ClinicalTrials.gov (register no. NCT01086618).¹⁹ Nonetheless, due to unknown reasons, it seems that the study has been suspended.

Whether due to the lack of homogeneity when comparing patient groups or to the limitations of the designs used to be able to provide evidence, the current dilemma persists and the debate continues.

Do patients with CRC and asymptomatic synchronous metastases benefit from the resection of primary tumors with regard to longer survival or better quality of life? Or, is there no benefit at all?

Considering the increased prevalence of colorectal cancer and the important percentage of patients who are diagnosed with stage IV tumors with unresectable metastases, the question could be answered by multi-center projects involving multidisciplinary groups with experience in the treatment of colorectal cancer. This is the only way to provide evidence regarding a controversial topic with high impact in our society.

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Received 7 May 2013

Accepted 8 May 2013

2173-5077/\$ – see front matter

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