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Research article

How to approach rectal carcinoma with potentially resectable synchronous hepatic metastases role of medical oncology

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Introduction

Colorectal cancer (CRC) is the third most frequent malignant neoplasm worldwide, representing the third cause of cancer death in both genders [1]. Approximately 20 to 34% of patients with RCC have hepatic metastases at diagnosis [2,3]. In rectal cancer (CR) with synchronous hepatic metastasis, surgery is the only potentially curative treatment. Survival at 5 years of patients submitted to curative resections varies between 35 and 58% according to the different series. However, only 20% of patients are candidates for curative surgery [4].

The Oncologist Approach

In the patient with synchronous hepatic metastases, the holistic approach of the patient is fundamental; the patients performance status, their complaints, their comorbidities, their preferences and the treatment goals will determine the sames [5]. CR patients with potentially synchronous resectable liver metastases are those who, if they respond to a conversion chemotherapy (CQ) scheme, may become resectable. These are the patients for whom intensive treatment is appropriate with the goal of cytoreduction (tumour shrinkage) and conversion to resectable disease [5].

CQ also allows patients to be selected because the patient responding to QC is the one most likely to be cured/surgery. CR with potentially resectable synchronous hepatic metastases after CQ, in case of response, can be treated with synchronous or delayed surgery. Subsequently most patients are candidates for complementary chemotherapy. The decision to perform radiotherapy short or long term regimen is controversial [6], the same occurring with surgery times, being, as previously mentioned, dependent on the patient, their comorbidities and also the from the center's experience.

The possibilities of combinations for CQ are extensive: doublet regimens (the most usual - oxaliplatin or irinotecan associated with fluoropyrimidine) or triplet regimen (in selected patients, with oxaliplatin and irinotecan associated with fluoropyrimidine) associated or not with biological agents, according to the state mutation of the RAS oncogene and, in some cases, also the determination of BRAF. In wild-type RAS tumors the association of anti-Epidermal Growth Factor Receptor (EGFR) to classical chemotherapy demonstrated increased rates of liver resection and also resection of the primary tumor. In mutated RAS tumours the association of bevacizumab (Vascular Endothelial Growth Factor receptor- VEGFR) with chemotherapy should be considered. The use of the triplet regimen associated with bevacizumab is increasingly considered in the RAS and BRAF tumours, since the BRAF mutation is predictive of poor prognosis [6].

Many studies have been performed to evaluate the response rate (RR) obtained from CQ and also the rate of hepatic resection with negative margins (R0). However most of them included CCR with initially unresectable hepatic metastases. The most important studies two phase II randomised trials where it was possible to analyze retrospectively that intensive treatment allowed better response rates and consequently better hepatic resection (R0) and better prognosis [7].

The first one was a Chinese prospective, randomised, Chinese trial where better RR and R0 resections were observed in the doublet with the anti-EGFR [8]. The second trial was an European, multinational, open-label, phase II OLIVIA trial, and in the group of patients treated with the triplet and anti-VEGFR, better RR and R0 resection were observed retrospectively (Table 1) [9].

Table 1. RR and Hepatic Resection in CCR with potential hepatic synchronous metastases.

Reference	Chemotherapy	n	RR %	Hepatic Resection (R0) %
[8]	FOLFIRI/FOLFOX ± cetuximab	116	57 *vs* 29	26 *vs* 7
[9]	FOLFOXIRI + bevacizumab vs FOLFOX + bevacizumab	80	81 *vs* 62	49 *vs* 23

Future

The decision of which scheme to use, the surgical and radiotherapy options are increasingly personalized for each patient and his illness. There is no definite overall therapeutic strategy for these patients. The decision of each individual clinical case and each person should be done in a multidisciplinary team philosophy, respecting the technical/surgical and the oncological criteria [5].

The identification of biomarkers is crucial in order to provide the best treatment, with increased overall survival and also provide the greatest quality of life possible for each individual patient.

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