Guidelines for the detection and treatment of liver metastases of colorectal cancer


Abstract The spread of the surgical treatment for hepatic metastases have been crucial in the improvement of treatment and survival of metastatic colorectal cancer. The early and accurate diagnosis of metastases and the assessment of their size are essential factors to reach the optimal results with this treatment strategy. The precise indication of the surgical technique with or without the previous administration of neoadjuvant chemotherapy is of significant importance for the choice of R0 surgery and the timing of intervention. Although there is an agreement regarding some parameters related to diagnostic techniques and surgical criteria such as the bilobar extension, the size of the remaining liver post-surgical removal and the indication of pre-operative chemotherapy, it is necessary to consider all these factors to set up standard criteria and optimize the results. In this article we review all these parameters, from disease follow-up to detect metastatic dissemination to the basic criteria for use of neoadjuvant chemotherapy, in order to suggest some general recommendations of evidence level II and recommendation grade A.

Key words Colorectal cancer • Liver metastases • Surgical treatment • Neoadjuvant chemotherapy

Introduction

The ultimate objective in cancer treatment is not a 5-year survival but a definitive cure. To consider a total cure in a treated cancer patient, one needs to achieve the same period of disease-free survival as that expected in a cancer-free population of the same age group. Reaching this objective would require an early diagnosis, a radical treatment with intention to cure and a regular systematic follow-up after the initial treatment. This follow-up would allow the detection of any relapses in curable situations. Such a possibility of achieving a total cure, therefore, puts into question the utility of diagnostic explorations used to detect curable relapses.

In colon cancer patients that have undergone radical surgery with the intention to cure, the follow-up is used to detect new primary tumours, pre-cancerous polyps and early relapses that will allow optimum treatment, which in the case of liver metastases can reach a 5-year survival rate of up to 40%.

The recommendations from the Treatment of Digestive Tumour (TTD) group with the collaboration of a panel of expert surgeons and radiologists for the early detection of hepatic metastases (HM) are collected in this document, starting with the right follow-up of patients from the primary tumour surgery. All recommendations are evidence level IIA unless otherwise indicated.

Follow-up for the detection of stage II and III relapses

Colon cancer disseminates “compulsorily” via the blood circulation through the liver, and from there it may dis-
seminate to the lungs, endocrine system and the brain. In the lower rectum, the dissemination may occur without the participation of the portal system through the haemorrhoidal plexus. The incidence of pulmonary metastases, in the absence of HM, is lower than 5%, whilst the incidence of bone and brain metastases is <1%. Another factor to take into account is the disease stage. What is the risk of relapse or metastases in stage I or IIa patients? Is it necessary to perform exploratory tests, other than colonoscopy, to detect secondary neoplasias in these patients? The heart of the matter is to establish the degree of risk one is prepared to take with respect to the detection of relapses, before any symptoms appear. Evidently, for stages I & IIa, the risk is lower than 10% and the follow-up gain is minimal.

In colon cancer, the first dissemination stage is the liver. Therefore it is not difficult to choose a liver ultrasound (US) scan or abdominal computerised tomography (CT) scan as the radiological test for a follow-up. If one is dealing with the lower rectum, one must watch out for pulmonary metastases by performing a thorax CT scan. Those tumours that, like colon cancer, express tumour markers, offer a great diagnostic advantage. The routine detection of carcinoembryonic antigen (CEA) is a simple laboratory test, able to detect a relapse, particularly in the liver. Detection before the appearance of symptoms should therefore lead to a higher rate of treatment success. In the case of colon cancer, standardisation of the multidisciplinary treatment of the liver metastases will favour the cure rate the sooner the diagnosis is done. Therefore it is necessary to determine not only the type of test but the time intervals and duration.

The theoretical duplication time for colon tumours is only 13.5 days in culture medium, but in the normal clinical practice this rate is multiplied by approximately 10 times, and so we would be looking at a duplication time ranging between 80 and 120 days. With this in mind, the “ideal” follow-up should therefore be every 3 months. The frequency of hospital visits is another aspect to consider, both in terms of the increased burden to the out-patient clinic as well as from the patients’ perspective, which may increase anxiety levels unnecessarily, particularly in those patients in the low-risk group.

On the other hand, the variability of the risk according to the disease stage should be contemplated within the current recommendations, however, none of the current guidelines (ASCO, ESMO, NCCN) clearly contemplate this variable.

\[\text{Table 1 Minimum follow-up according to relapse risk}\]

<table>
<thead>
<tr>
<th>Lower risk</th>
<th>High risk</th>
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<tbody>
<tr>
<td>Stages I and IIa</td>
<td>Stages IIb and III</td>
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<tr>
<td>List of symptoms\textsuperscript{a}</td>
<td>List of symptoms</td>
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<tr>
<td>Clinic+CEA test annually for the first 2 yrs</td>
<td>Clinic+CEA test 6 mthly+abdominal CT 6 mthly for the first 3 years. Then annually up to 4th–5th year.</td>
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<tr>
<td>Colonoscopy\textsuperscript{a} 1st, 3rd and 5th years</td>
<td>CT thorax 6 mthly if lower rectum is involved and annually for the rest up to 5 years. Colonoscopy 1st, 3rd and 5th years\textsuperscript{b}. Proctosigmoidoscopy 6 mthly if rectum involved and no pelvic radiation performed\textsuperscript{c}.</td>
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\textsuperscript{a}Instruct patients about alarm symptoms.\textsuperscript{b}Annually if polyps observed. Every 5 years if they are hyperplasic.\textsuperscript{c}It should be done before 6 months if pre-surgery examination was not complete.

Primary tumour post-resection follow-up guidelines

Taking into account current guidelines from ASCO 2005 and other medical societies, and Spanish experience in following-up and treating liver metastases, we recommend a minimal follow-up for patients in stages I and IIa, and more intense for stages IIb and III, which includes clinical visits, CEA testing every 3 months, abdominal CT scan every 6 months (plus thoracic CT scan if lower rectum is involved) and annual thoracic CT scan for the reminder cases. We recommend proctosigmoidoscopy every 6 months in cases where the rectum is not irradiated [1–6] (Table 1).

Follow-up after the resection of liver metastases

At present, there is no published work reviewing or doing meta-analysis on follow-up studies of patients that have undergone resection of liver metastases. However, being an advanced cancer situation, whether the patient undergoes chemotherapy treatment or not after surgery, it is clear that the follow-up must be intensive. If the patient is marker positive, testing every 3 months for markers during the following 2 years must be done. Thoracic CT scan must also be included in the follow-up of these patients.

We recommend a first follow-up visit (whether or not post-surgical chemotherapy is used) at 3 months after surgery, to test for CEA and to perform an abdominal CT scan. Then, we recommend 6-monthly visits to test for CEA and to perform an abdominal CT scan, and...