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Liver resection in metastatic colorectal cancer: a multidisciplinary approach

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ABSTRACT

Aim: to analyze qualitative short-time results of a new program for multidisciplinary liver evaluation in complex cases of liver metastasis from colorectal cancer.

Patients and methods: 40 clinical consecutive evaluations with liver metastasis assessed for major liver resection by a multidisplinary specialist committee. Complementary explorations performed included CT and ultrasounds, and MRI or PET for doubtful cases. Liver resection was made in a single operation or two-stage hepatectomy, or combined with other techniques.

Results: postoperative mortality at 30 days was 4%. Complications occurred in 28%, with surgical wound infection being most frequent (20%); 16.6% of resections were transfused, with a mean volume of 1000 ml. Two patients needed reoperation –one for an intraperitoneal abscess and one for bile-duct stenosis. Percentage of global relapse was 36%, with 26% of relapses out of the liver. Actuarial survival at one year follow-up was 90%, and 82% at two years; 64% of patients remain free of disease two years after the operation.

Conclusions: programs for liver resection for colorectal cancer metastasis may be implemented by multidisciplinary teams of recent setup. There is a need to evaluate own results and then compare them with a standard of quality previously reported.

Key words: Liver metastasis. Colorectal cancer. Surgery.

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INTRODUCTION

Colorectal cancer is the most frequent digestive cancer in West Europe and the United States; in our country, it has an incidence of 20-30 cases per 100.000 persons/year (near 18.000 new cases each year) with slight regional variations, and it is the cause of 20% of deaths from malignant disease (1,2).

The development of liver metastasis involves the evolution of colorectal adenocarcinomas in 30-50% of patients (3,4). These may be synchronic metastases, found at the same time that the primary tumor, in 10-25% of cases; the rest are metachronic metastases, found during tumor follow-up.

Colorectal cancer has an overall survival lower than 60% at five years. In patients with liver colorectal metastasis with no treatment, a short survival of 4 to 9 months may be expected, although in selected patients, survival periods of about 24 months can be reached. In recent years, with the association of liver metastatic resection with curative intention, we have improved long-term and mid-term survival, this being of 20-40% at 5 years, with low morbidity and mortality.

Improved survival using curative liver resection for liver metastasis from colorectal cancer may due to a number of reasons: a better selection of patients undergoing hepatic resection; liver resection when metastatic disease is controlled, tumor sensitivity to new chemotherapeutic agents like oxaliplatine and irinotecan, and better monitoring of the tumor process, as well as a combination of other techniques with surgery, and the multidisciplinary approach.

The aim of this study was to analyze the qualitative results of a program for multidisciplinary liver evaluation in complex cases of liver metastasis from colorectal cancer.

PATIENTS AND METHODS

Forty consecutive clinical evaluations of patients with liver metastasis from colorectal cancer liable to major he-

patic resection were analyzed. Evaluations were made by a specialist committee: hepatic surgeon, hepatologist, oncologist, radiologist, and pathologist.

For clinical decision-making, liver metastases were evaluated with ultrasounds and triphasic helical CT, with MRI being reserved for doubtful cases. The aim of radiological explorations was to establish the diagnosis of liver tumor, and the number, size, location of metastases and their relation to vascular structures, as well as to detect the possibility of extrahepatic malignant disease. PET was considered when suspicion of malignant disease was high and no tumor image was found using radiological techniques.

In all patients an intraoperative liver ultrasound was performed to rule out minor liver tumors not seen in previous explorations. A wide colonoscopy was performed when none had been carried out during last year.

Coexistent liver metastases and extrahepatic malignant disease was carefully evaluated by the committee to define the order of treatments: generally, two-stage surgery with liver resection in the last stage was recommended. Unresectable extrahepatic disease contraindicated liver resection.

When major liver resection was indicated, a liver volumetry with helical CT was performed in order to analyze the volume of remnant liver, which should be higher than 25% and 40% for cases of fatty liver or previous chemotherapy. If necessary, a two-stage hepatectomy was indicated, with first a minor resection followed by a major resection after chemotherapy and compensatory hypertrophy, as well as the performance of liver resection combined with other techniques such as portal occlusion or radiofrequency ablation.

All patients were treated with systemic chemotherapy as an adjuvant to liver resection. Neo-adjuvant chemotherapy was indicated when hepatic resection was not safe or a non-radical resection was suspected. This previous chemotherapy may be associated with treatments combined with liver resection.

RESULTS

In 15 of 40 evaluations by the committee, systemic chemotherapy was considered the best treatment with palliative intention. In 25 cases resective surgery with radical intention was indicated, using liver resection alone or in combination with other techniques, or two-stage hepatectomy.

Operations performed

Resective liver surgery was indicated in 25 cases (62.5%) –3 were excluded during the procedure by unsuspected findings that made it impossible to perform a radical intervention. In 18 cases a liver resection was performed including two or more segments; in 4 cases surgical non-resective techniques were performed as a treatment previous to later radical liver resection (Fig. 1).

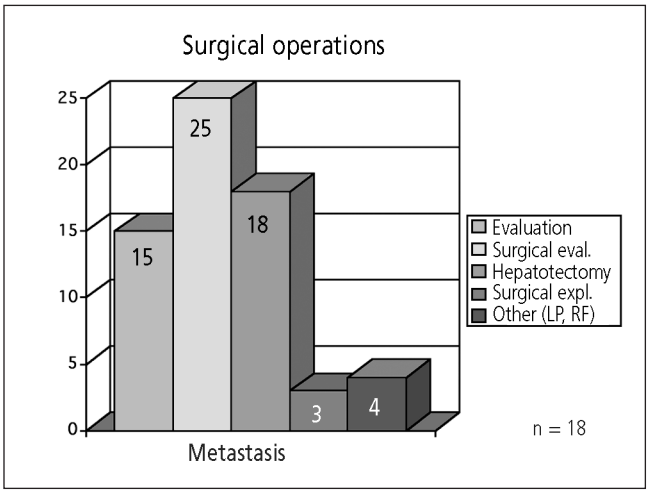

Fig. 1. Overall evaluations for liver resection.
Total de evaluaciones tributarias de resección hepática.

In 10 cases a single hepatectomy was made (55.5%), while in 8 cases it was necessary to combine liver resection with other techniques: right hepatectomy with previous portal ligature in two cases, combined radiofrequency ablation, and two-stage hepatectomies (Figs. 2 and 3).

The most frequently performed anatomical resection was right hepatectomy (38.8%) followed by left hepatectomy and left lobectomy (11.1% each one). Plurisegmentectomy was necessary for 7 cases (Figs. 2 and 3). One case had extrahepatic disease at diagnosis, with liver metastasis and local anastomotic recurrence of the primary tumor; in this case, the first intervention was a radical

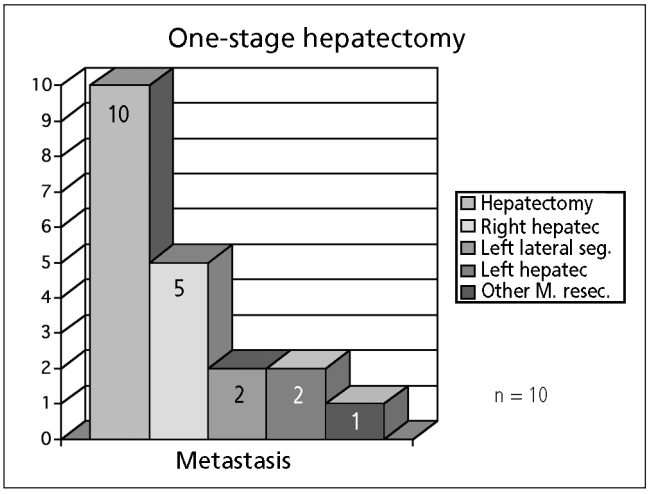

Fig. 2. Type of liver resection in one-stage hepatectomy.
Tipos de resección realizada en la hepatectomía como gesto único terapéutico.

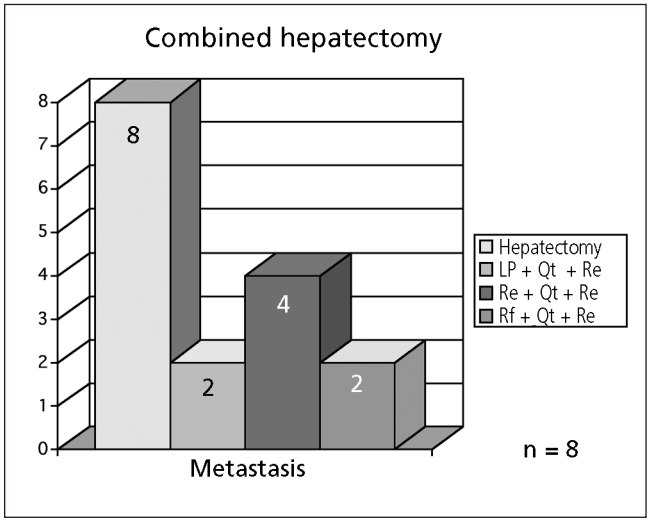

Fig. 3. Combination of liver resection and other techniques in the same procedure or a later reoperation (LP: portal ligature; Qt: systemic chemoterapy; Rf: radiofrequency; Re: liver resection).
Combinación de la hepatectomía a otras técnicas o realización de la misma en dos tiempos. (LP: ligadura portal selectiva; Qt: quimioterapia sistémica; Rf: radiofrecuencia hepática; Re: resección hepática).

resection of colorectal disease, with hepatic resection in a second operation.

In spite of an intraoperative study using ultrasounds and a careful surgical technique, a histological study evidenced focal invasion of the margins in 2 cases (11.1%).

Patient characteristics

Median age for the 18 operated patients was 66.7 years (range 41-84). Most were men (77.7%). The primary tumor was rectal in 16.6%, and colonic in 83.3%, from the sigmoid colon in 50% and the right colon in 33.3%. The classification of colorectal tumors according to Duke's stages was: A in 1 case (5.5%), B in 6 (33.3%), and C in 11 (61.2%) cases. The presentation of metastatic disease was synchronic with the primary tumor in 66.6% of patients, and metachronic in the rest. In these metachronic liver metastases, the median time of surveillance after primary resection and detection of metastatic disease was 18.6 months (range 17-25). CEA prehepatectomy value was normal in one case, between 5-10 ng/ml in other case, and higher than 10 ng/ml in 11 cases (no determinations in 3 cases from other hospitals).

Liver metastases were single in 3 cases (16.7%); between 2 and 4 metastases in 10 cases (55.5%), and 5 or more tumors in 5 cases (27.8%). Median number of liver tumors was 3.2. In 8 cases metastases were bilobular at diagnosis.

Postoperative morbidity-mortality

Global postoperative mortality in the first 30 days was 4%, 5.5% in cases with liver resection. There was a death from postoperative liver failure and severe coagulation disturbances.

Median postoperative stay at hospital was 8.5 days (range 3-25). Of 18 liver resections 28% (5 cases) had complications, with surgical wound infection being most common (20%). Blood transfusion was necessary in 4 patients (16.6%) during the operation, always in major liver resections, with a median blood volume of 1000 ml. In 2 cases a reoperation was needed (11.1%), in one for an intraabdominal abscess and in one for hepatic duct stenosis.

Relapse and survival

The aim of the study was to assess the safety of the liver evaluation and liver resection program, and follow-up reached 24 postoperative months. Median surveillance of patients has been 15 months (range 5-24).

Actuarial survival rates in patients with liver resection were 90% within the first year and 82% at two years. Overall percentage of relapses was 36% (free-of-disease survival at two years, 64%), with the earliest relapse developing at 9 months (extrahepatic, in site of primary resection). Extrahepatic relapse was most frequent (26%, 9% intrahepatic).

Perioperative and postoperative chemotherapy

In 8 of 40 evaluated patients neo-adjuvant chemotherapy to liver resection was indicated in order to consider unresectable liver tumors or tumors with a high probability of minor free margins in the resection (less than 1 cm). Good clinical and radiological-CT responses to chemotherapy were obtained in 6 patients (75%). Of these 6 patients, 4 were reassessed and considered for surgical resection (50%), with a successful radical liver resection. Two patients with a poor response to chemotherapy were not referred for surgery and were followed using a second-line chemotherapy. The other cases are in evaluation by the committee.

In all cases systemic chemotherapy was based in 5-FU and oxaliplatine for first line, and in 5-FU plus irinotecan for second line of treatment. All patients received postoperative chemotherapy during 4-6 months.

DISCUSSION

Last year's experience in liver resection for colorectal metastasis demonstrates that surgery is an effective treatment with acceptable morbidity-mortality (5-8). Somehow, up to 50% of operated patients will have a relapse of disease in the remaining liver or other extrahepatic locations (9-11).

In selected patients, resective surgery as single treatment offers excellent results, with 5-year survival being as high as 40% (12-14). Considering the absence of other therapeutic alternatives with curative possibilities, hepatectomy must be considered for other patients when a radical resection of hepatic and extrahepatic tumor disease is possible with a low morbi-mortality (5,9).

A correct identification of candidates needs good presurgical staging (15,16) and an intraoperative evaluation based on liver ultrasounds (17). In our group, intraoperative ultrasounds offers up to 30% of unsuspected findings and changes surgical plans in about 15%, rejecting liver resection in 10%.

During the past few years life expectancy for patients with liver metastasis from colorectal cancer has improved due to relevant advances in chemotherapy, mainly the incorporation of oxaliplatine and irinotecan, and the introduction of new treatment modalities such as continuous 5-FU infusion. With these new therapeutic modalities we can elicit responses in about 50% of liver metastases. Chemotherapy can be adjuvant (in the postoperative period) or neo-adjuvant, i.e., previous to liver resection. Patients with unresectable tumors in view of impossible-to-obtain free margins or of several risk factors for relapse may benefit of neo-adjuvant chemotherapy with the aim of reducing tumor mass and of making unresectable tumors resectable, thus reducing the postoperative risk of tumor relapse.

Deliberate surveillance after curative liver resection with CEA, simple chest radiology, and abdominal CT makes early detection of relapse possible. Intensive surveillance is worthwhile for survival as it allows a new radical resection in about 17-33%, depending on tumor site (18). Survival after radical resection of intrahepatic relapsed tumors is similar to that of first radical liver resection, so re-resections must be indicated in the same way as primary liver resection (19).

The results from our group are similar to those previously published regarding morbidity and mortality, the quality parameters considered as a standard by groups treating this problem. Mortality must be below 5%, and it was 4% in our series all operations considered, and 5.5% when only liver resections are evaluated. Overall morbidity must be under 30%, and we found a global rate of complications of 28% in our series (most frequent being surgical wound infection, 20%). Need for blood transfusion was low (16.6%) when compared to the values around 30-50% found in the literature.

Considering the results of this initial phase of the program for liver resection with a two-year surveillance, we feel that we must go on along these same lines, and promote actions allowing an improvement of long-term results. Actuarial survival is about 90% at year 1, and 82% at year 2, similar to series accepted worldwide (13). We must wait for our 5-year surveillance to evaluate whether our overall 5-year survival is standard –about 25-40%.

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