Report

Surgical treatment of hepatic metastases from breast cancer

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Summary
We have performed a retrospective study to evaluate whether surgical treatment is beneficial in patients with hepatic metastases from breast cancer. Between September 1985 and September 1998, 25 patients with hepatic metastases (14 solitary and 11 multiple), eight of whom had extrahepatic metastases, underwent hepatectomy. All of the detectable liver metastasis were resected in all of the cases. There were no severe postoperative complications. All but one of the patients received adjunctive polychemotherapy after the hepatectomy. After the hepatectomy, recurrent tumors were detected in 18 of the patients, being located in the liver in 12 (67%) of them. Overall, however, hepatectomy ensured that the liver was clinically recurrence-free for a median of 24 months (range 2–132 months). Eleven patients died of recurrent tumors, two died of other causes and the remaining 12 are currently alive. The 2- and 5-year cumulative survival rates after hepatectomy were 71% and 27%, respectively, and the median survival duration was 34.3 ± 3.2 months, much better than the period of 8.5 months for another series of patients treated with standard or non-surgical therapies at our institution. The number and the size of hepatic metastases, the interval between treatment of the primary lesion and hepatectomy, and the existence of extrahepatic metastasis were not adverse prognostic factors. In conclusion, our data, although limited and highly selective, suggest that surgical treatment of hepatic metastases from breast cancer may prolong survival in certain subgroups of patients to a greater extent than standard or non-surgical therapies.

Introduction
The occurrence of liver metastases in patients with breast cancer confers a poor prognosis, despite the use of systemic chemotherapy with or without regional chemotherapy [1–7]. Only the presence of brain metastases confers a poorer prognosis. Some patients have responded to conventional treatments, but the responses are invariably short-lived [4]. A number of treatments, including intra-arterial infusion chemotherapy [6–8] and regional immune therapy [9], have been attempted in order to improve the prognosis, but a standard treatment procedure has yet to be established.

Surgery has seldom been the treatment of choice, because the occurrence of hepatic metastases is considered to be a manifestation of systemic disease. However, several preliminary studies of surgical treatment have been carried out [10–17] and some of them have yielded unexpectedly promising results. We hypothesized that hepatectomy, used as a cytoreductive treatment, might improve the survival of patients with hepatic metastases from breast cancer. In this article, we report our experience with 25 such patients whose hepatic metastases were resected and discuss the survival benefits of this surgical procedure.

Patients and methods
For detecting liver metastasis after treatment of primary breast cancer, abdominal ultrasonography was performed every 6 months and tests for the tumor markers CEA and CA15-3 were done every 2 months in our routine follow-up protocol. If the presence of liver metastasis was suspected, a further detailed in-
vestigation using CT scanning, magnetic resonance imaging and/or angiography was done in order to confirm the diagnosis and to evaluate the feasibility of surgery. When the liver metastases were considered totally resectable and there were no serious metastases in organs outside the liver such as the brain, lung, pleura or peritoneum which were rapidly growing and/or life threatening, we judged the patient to be eligible for hepatectomy on condition that her general condition enabled her to tolerate hepatectomy. Obviously, hepatectomy was contraindicated for diffuse ill-defined liver metastasis.

Between September 1985 and September 1998, hepatectomy was performed in 25 women with breast cancer in order to resect their hepatic metastases. The clinical status, treatment methods and patient outcomes are listed in Table 1.

The mean age of the patients was 51.3 years (range 27–70 years). The liver was the first site of recurrence in 19 patients, four of whom had Stage IV breast cancer involving the liver. The other sites where metastases developed prior to liver metastases were the bone, local skin, and supraclavicular lymph nodes in three, two and one, respectively. Simultaneous bone and liver metastases were discovered in two patients. The mean interval between the operation for the primary lesion and the occurrence of liver metastasis was 31.9 months (range 0–120 months). The treatments administered prior to hepatectomy were transarterial chemoembolization, chemoendocrine therapy, wide local skin excision for local metastasis and radiotherapy for supraclavicular lymph node metastases in six, two, two, and one patients, respectively. At the time of hepatectomy, metastases were found to be limited clinically to the liver in 17 of the patients. The mean interval between the discovery of liver metastasis and hepatectomy was 4 months (range 0–19 months). In the two patients who received chemoendocrine therapy, more than a year elapsed from the discovery of hepatic metastasis to hepatectomy. One 27-year-old woman in whom liver metastases were discovered during pregnancy underwent hepatectomy at 20 weeks of pregnancy in order to avoid systemic chemotherapy (case 23).

Prior to hepatectomy, not only visual and manual examinations by the surgeon but also detailed intraoperative ultrasonographic scanning of the liver surface using a special probe was used in order to make the final decision about hepatectomy and the incision line. In fact, we sometimes found other metastatic lesions as well as those revealed preoperatively in several cases, but we did not have to abandon hepatectomy in any of the patients during the operation.

The operative procedures performed were right hepatectomy in four patients, left hepatectomy in three, extended left hepatectomy in four, lateral segmentectomy in one, and 17 segmental resections in 13. Two patients underwent radical mastectomy at the same time. Lymph node sampling at the hepatic pedicle, and around the common hepatic artery was carried out in 19 and radical dissection of lymph nodes was extended over the para-aortic region in three. In every patient, all the detectable liver tumors were resected. The mean operative duration was 4 h, and the mean blood loss was 680 ml. Only five patients needed blood transfusions and no serious postoperative complications occurred.

The post-hepatectomy treatment given was not uniform; all but one of the patients received some form of systemic polychemotherapy with or without intraarterial chemotherapy using an infus-a-port (Table 1). The main regimens were CMF (cyclophosphamide, methotrexate and 5-fluorouracil), CAF (cyclophosphamide, adriamycin and 5-fluorouracil), and/or taxotere. Trans-arterial continuous infusion chemotherapy using 5-fluorouracil was given to four of the patients, who also received the regimens of CMF or CAF. More recently, three young patients were given high-dose chemotherapy (HDC) supported by peripheral blood stem cell transplantation (PBSCT) and five received taxotere.

Survival was calculated from the dates of hepatectomy or detection of hepatic metastases to the date of death or the last observation, and survival curves were plotted using the Kaplan–Meier method. Possible prognostic factors after hepatectomy, including the interval between treatment for the primary lesion and liver metastasis, clinical manifestations of extrahepatic metastases, number of liver tumors, the biggest size of liver metastases in each patient and the presence of lymph node metastasis in the abdomen were also examined. The log-rank test was used to evaluate the significance of differences between survival curves.

Results

All 25 patients had histologically proven metastatic liver disease from cancer of the breast. Fourteen had a single metastasis, three had two, four had three, and four had multiple metastases. Two patients had mul-