Surgery for liver metastases from breast cancer

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Abstract
Liver metastases develop in approximately half of women with metastatic breast cancer, and are typically associated with metastases at other sites, indicating advanced disease and poor prognosis. Whenever possible, hormonal therapy should be administered, until resistance develops. Several series in the literature have reported a poor effect of chemotherapy alone in patients with metastatic breast cancer, therefore liver surgery could be considered as an adjuvant treatment to systemic therapy in highly selected patients. This study looked at recent case series in the literature, and analysed prognostic factors and indications for surgery.

Key Words: Breast cancer, liver metastases, hepatic resection

Background
Liver metastases (LMs) develop in approximately half of women with metastatic breast cancer (MBC), and are typically associated with metastases at other sites, indicating advanced disease and poor prognosis [1]. Isolated LMs appear in only 4–5% of patients with MBC [2–4]. Systemic chemotherapy or hormone therapy (or both) is usually indicated for these patients.

The standard approach to patients with newly diagnosed MBC is to determine the extent of the metastatic disease and whether there are sites of disease that require urgent treatment. After this initial evaluation, the key question for the clinician is whether the patient is likely to benefit from hormonal therapy. Whenever possible, hormonal therapy should be administered, until resistance develops [5]. Several series in the literature have reported a poor effect of chemotherapy alone in patients with MBC [4,6,7]. Currently, with the recent chemotherapy regimen, the median survival of such patients is close to 24 months [8].

Because complete response of LM to chemotherapy or hormone therapy is very rare, liver surgery could be considered as an adjuvant treatment to systemic therapy in highly selected patients. Publications concerning surgery for breast LMs remain anecdotal and this surgery is still controversial because the presence of LMs reflects the presence of disseminated disease, in which a local treatment modality is of doubtful value [6]. In fact, this is true for any metastatic tumour, notably for colorectal LM, for which hepatectomy has clear indications.

Improvements in surgery and anaesthesiology, resulting in a reduction of mortality and morbidity, have allowed extension of the indications for hepatic resection [9,10], and the first series reporting hepatectomy for breast cancer patients was published in 1991 [3].

Results
Does liver resection result in an increase in survival? Clearly the answer is yes in selected patients [11]. Series reported in the literature show (when considering only the series reporting at least 10 patients) favourable 5-year overall survival rates ranging from 18% to 61% and a median overall survival reaching 57 months for curative resection (Table I) [1,11–18]. With classic non-operative treatment, there is no living patient at 5 years.

Prognostic factors
Prognostic factors in MBC are difficult to validate after liver resection owing to the small numbers of...
patients involved. Some authors report that the interval between diagnosis of the primary cancer and LM was statistically correlated with survival. So, Pocard et al. [14] reported that survival at 36 months was 55% when LM occurred in <48 months versus 85% when LM occurred after 48 months \( (p = 0.01) \), and found that it was the only parameter statistically correlated with survival. Elias et al. [11] found that the only significant prognostic factor for survival was the hormone receptor status, with a median survival of 44 months when positive and 19 months when negative \( (p = 0.01) \). The hormone receptor status is classically one of the main prognostic factors in any study concerning survival of patients with breast cancer. In the report by Sakamoto et al. [18], the presence of extrahepatic disease prior to hepatectomy was the only significant prognostic factor and the 5-year survival rate of the patients without extrahepatic disease was 31% versus 21% \( (p = 0.027) \).

It is fundamental to underline that in none of these series, neither the extent of the liver disease (the number and the maximal size of the LM), nor the presence of positive hilar lymph nodes (present in 33% of the cases) [11], had a significant prognostic impact on overall survival. This suggests that hepatectomy for LM is only a cytoreductive surgery, and cannot be considered as a definitive and isolated treatment.

### Indications

Definitive conclusions cannot be drawn because of the limited and selected number of cases of these series; however, this approach represents a valid cytoreductive procedure for many patients with isolated LM and may be curative for some of them. Only a prospective multicentric randomized study will demonstrate definitively whether surgical resection can really improve long-term survival rates in patients with isolated LM with or without systemic chemotherapy, compared with other methods of treatment.

At this time, it appears useful and logical to propose hepatectomy for women with MBC when the three following conditions are absolutely confirmed: (1) a low operative risk (this contraindicates a complex and risky hepatectomy), (2) the LM is completely resectable (this cytoreductive surgery must be maximal and supraradical), (3) no extrahepatic disease (except for bone metastases which are easily controlled with radiotherapy) [14]. The decision is straightforward for young women. For older women, the negative hormone receptor status acts as a relative contraindication to hepatectomy [11].

Moreover, new systemic treatment will probably modify this scheme and must be tested in association with hepatectomy. In fact the general landscape of endocrine therapy and chemotherapy has recently been modified by the adjunct of new potent drugs (last generation of aromatase inhibitors, taxanes, heceptin), leading to new therapeutic schemes in metastatic breast cancer [5].

In conclusion, the surgical treatment of LM must be considered as one part of a multimodal treatment of the metastatic disease. It is of real benefit for a few patients, and should be used more extensively in the future.

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