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Original Research

Surgical resection versus systemic therapy for breast cancer liver metastases: Results of a European case matched comparison

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Abstract ***Background:*** Resection of breast cancer liver metastases (BCLM) combined with systemic treatment is increasingly accepted but not offered as therapeutic option. New evidence of the additional value of surgery in these patients is scarce while prognoses without surgery remains poor.

Patients and methods: For this case matched analysis, all nationally registered patients with BCLM confined to the liver in the Netherlands (systemic group; N = 523) were selected and compared with patients who received systemic treatment and underwent hepatectomy (resection group; N = 139) at a hepatobiliary centre in France. Matching was based on age, decade when diagnosed, interval to metastases, maximum metastases size, single or multiple tumours, chemotherapy, hormonal or targeted therapy after diagnosis. Based on published guidelines, palliative systemic treatment strategies are similar in both European countries.

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Results: Between 1983 and 2013, 3894 patients were screened for inclusion. Overall median follow-up was 80 months (95% CI 70–90 months). The median, 3- and 5-year overall survival of the whole population was 19 months, 29% and 19%, respectively. The resection and systemic group had median survival of 73 vs. 13 months ($P < 0.001$), respectively. Three and 5-year survival was 18% and 10% for the systemic group and 75% and 54% for the resection group, respectively. After matching, the resection group had a median overall survival of 82 months with a 3- and 5-year overall survival of 81% and 69%, respectively, compared with a median overall survival of 31 months in the systemic group with a 3- and 5-year overall survival of 32% and 24%, respectively (HR 0.28, 95% CI 0.15–0.52; $P < 0.001$).

Conclusions: For patients with BCLM, liver resection combined with systemic treatment results in improved overall survival compared to systemic treatment alone. Liver resection should be considered in selected cases.

1. Introduction

Approximately, 6–10% of breast cancer patients will present with metastatic disease at diagnosis and around 30% of women diagnosed with non-metastatic disease will relapse after treatment [1,2]. The incidence of liver-only presentation of distant metastases ranks third, averaging around 1–8%, after bone and lung metastases. Once metastatic disease is diagnosed, treatment is generally palliative and usually consists of systemic treatment only. This palliative approach has yielded median survival rates ranging between 3 and 16 months for all subtypes combined [3–5].

Resection of liver metastases is an established option in colorectal metastases but still remains controversial in metastatic breast cancer (BCLM) even for oligometastastic disease [6–8]. So far, only few small retrospective series have reported outcomes regarding the resection of BCLM with a median survival of 30–70 months and 5-year overall survival rates of 33%–50% [9–25]. At the Centre Hépato-Biliaire, Paul Brousse, Villejuif in France, selected patients with BCLM have routinely undergone surgical resection since 1985 with previously reported promising results [9].

The purpose of this study was to isolate the effect of liver resection when comparing liver resection for breast cancer metastases combined with systemic treatment (resection group) and systemic treatment only (systemic group) in two distinct population with similar European systemic treatment approaches that is based on the European Society of Medical Oncology International Consensus Guidelines for Advanced Breast Cancer [26]. For this purpose, the series of liver resection for breast cancer metastases from a specialised centre in France (Centre Hépato-Biliaire, Paul Brousse) was compared with population based data from the Netherlands Cancer Registry of patients treated with systemic therapy only [9,20,27].

2. Methods

2.1. Patients

All female breast cancer patients with liver metastases in the Netherlands between 2003 and 2013 and all consecutive female patients who underwent a partial hepatectomy at an experienced hepatobiliary centre in France between 1985 and 2012 were screened for inclusion in the study. Oligometastatic disease confined to the liver was the main criteria for inclusion for both systemically treated patients and systemically treated patients combined with liver resection.

2.2. Systemic group

All Dutch centres follow a national guideline, similar through the European Union, regarding treatment of breast cancer (liver) metastases and does not recommend hepatic resection as an option even in oligometastastic disease. In short, oestrogen receptor (ER) and progesterone receptor (PR) positive breast cancer are eligible for hormonal therapy. Chemotherapy is the treatment of choice if the hormone receptors are negative, hormonal therapy no longer appears to be effective, there is rapid disease progression, extensive and rapidly growing visceral metastases have developed (lung, liver, lymphangitis). In patients with a HER2-positive metastatic breast cancer, the combination of trastuzumab with other chemotherapy is first-line therapy ([28]).

Additional variables that are not part of the standard cancer registry i.e. number of metastases and maximum size of metastases were additionally collected in selected hospitals. Selection of these hospitals was based on volume of patients treated and approval from their board of directors. Data were extracted from imaging reports, patient notes, or correspondence by trained data managers of the Netherlands Cancer Registry (NCR).