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Large variation in the utilization of liver resections in stage IV colorectal cancer patients with metastases confined to the liver

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Abstract

Background: Surgical resection of both the primary tumor and all metastases is considered the only chance of cure for patients with stage IV colorectal cancer. The aim of this study was to investigate change over time in the utilization of liver resections, as well as possible institutional variations.

Patients and methods: All patients diagnosed with stage IV colorectal cancer with metastases confined to the liver (n = 1617) between 2004 and 2012 were selected from the population-based Eindhoven Cancer Registry. The proportion of patients undergoing liver resection was investigated. Institutional variation in the period 2010–2012 was analyzed using logistic regression. Kaplan–Meier and Cox regression analyses were used to analyze overall survival.

Results: The proportion of patients undergoing liver metastasectomy increased over time from 8% in 2004 to approximately 24% in 2012. There was a wide inter-hospital variation in the proportion of patients that underwent a liver resection (range: 14–34%) in the period 2010–2012. Liver resection was more often performed in younger patients and in rectal cancer patients. Median overall survival in patients undergoing liver resection was 55 months. Adjusted for potential confounders, resection of liver metastases was strongly associated with improved overall survival (HR 0.32, 95%CI 0.25–0.40).

Discussion: This study shows that despite the excellent long-term prognosis for patients with stage IV colorectal cancer after liver resection, there is still a large institutional variation in the utilization of this potentially curative therapy.

Keywords: Colorectal cancer; Metastases; Stage IV; Liver resection; Metastasectomy; Variation

Introduction

Colorectal cancer (CRC) is one of the most frequently diagnosed cancer types worldwide. In the Netherlands, approximately 2500 patients are diagnosed with colorectal cancer and synchronous metastases (stage IV) each year.[1,2] The prognosis of patients with stage IV disease has improved significantly over the last two decades, mainly because of an improved survival in patients with isolated liver metastases.[1–4]

For these patients surgical resection of the primary tumor and all metastases leads to a significant increase in long-term overall survival. Some twenty years ago, less than 5% of stage IV CRC patients underwent a liver

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metastasectomy.[3,4] Nowadays, this number has increased up to 15–20%.[3,4] It is estimated that resection of all liver metastases is possible in 20–30% of all stage IV CRC patients.[5] Resection of liver metastases is safe and can potentially cure patients, demonstrated by 30-day postoperative mortality of less than 2% in high volume centers and five year survival rates are around 50% in selected patients groups.[5–7]

In recent years, the criteria for resectability of hepatic metastases have expanded.[8] Currently, curative treatment is considered if the expected remnant liver is at least 30% of the preoperative volume, there are no unresectable metastases outside the liver, liver resection is anatomical possible with regard to vascular and biliary structures and the patient is fit for surgery.[9,10] New techniques, such as portal vein embolization and radiofrequency ablation, show promising long-term results.[11,12] The benefit of neoadjuvant systemic therapy in downsizing unresectable colorectal liver metastases has also been shown in various studies.[13]

A treatment plan is commonly achieved through consensus of a multidisciplinary team, consisting of the involved medical and surgical specialists. Nevertheless, it seems possible that depending on experience and knowledge the criteria on what constitutes resectable disease are interpreted differently by different specialists. Indeed, Young et al. showed that large differences in referral practice existed between hospitals in the United Kingdom for patients with liver metastases.[14] There was also a considerable difference in patients deemed operable between local colorectal specialist teams and a tertiary liver specialist team.[14] Even among liver specialists there seems to be a substantial inter-individual variation in the decision on whether or not metastases are resectable, highlighting the complexity of the decision making process.[15,16]

We hypothesized that this differences in referral practice and interpretation of resectability, might lead to a considerable variation in the proportion of patients with colorectal liver metastases who undergo a metastasectomy. The aim of this population-based study was to investigate the association between hospital of diagnosis and the utilization of liver resection in the south of the Netherlands in recent years.

Patients and methods

Patient selection

Population-based data were extracted from the Eindhoven Cancer Registry (ECR). This database includes all newly diagnosed cancer patients from ten hospitals in the south of the Netherlands. The ECR was founded in 1955 and currently covers a population of 2.4 million inhabitants. Registration is primarily based on notification by the nationwide automated pathology registry PALGA and the National Registry of Hospital Discharge Diagnosis. Data are retrieved from patient files by specially trained registration clerks from the Netherlands Comprehensive Cancer Organisation. Classification of tumor characteristics is done according to the TNM Classification of Malignant Tumors and International Classification of Diseases for Oncology. Follow-up consists of linking the ECR to the Municipal Personal Records database to retrieve information on vital status and date of death. At the time of data extraction, follow-up was completed up to December 31, 2013. As the ECR only registers data on primary tumors and their primary treatment, information on metachronous metastases is not recorded and thus also not included in this study.

Data selection

For this study, we selected all patients who were diagnosed with stage IV colorectal cancer with liver-only metastases between 2004 and 2012. The extracted data include patient, tumor and treatment characteristics. Socioeconomic status was estimated based on postal code of patients' residence at time of diagnosis, using data on income and education from the Netherlands Institute for Social Research. Location of the tumor was divided in colon (C18–C19) and rectum (C20). Year of diagnosis was defined as the year of first histological confirmation (most often from endoscopic biopsy). In the Netherlands, liver surgery is centralized in specific referral centers to ensure the best quality of care. When liver metastases is considered a possibility by the local multidisciplinary colorectal teams, patients from the general hospitals are referred to the multidisciplinary liver teams in these expert centers to assess eligibility. Two out of ten hospitals in the region included in this study are referral centers, these hospitals are indicated as 'liver center' in the analyses. The ECR only provides information on whether or not a patient underwent a liver resection, but does not register if a patient was referred to a multidisciplinary liver team and considered not eligible for liver surgery.

Data analysis

All patients were classified according to surgical treatment strategy: (1) patients who underwent neither a resection of the primary tumor nor a metastasectomy, (2) patients who underwent only resection of the primary tumor, and (3) patients who underwent resection of both the primary tumor and metastases. The ECR does not provide information on the number of metastases, nor on treatment per metastatic lesion; thus, in patients with multiple liver metastases, it cannot be confirmed with complete certainty that metastasectomy was performed for all metastases. Patients who received radiofrequency ablation as stand-alone treatment for metastases were not included in the 'resection of both primary and metastases' category. Because of the small number of patients, patients who