



Short term and long term results of patients with colorectal liver metastases undergoing surgery with or without radiofrequency ablation

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Accepted 14 January 2016

Available online 23 January 2016

Abstract

Purpose: The combination of resection and radiofrequency ablation (RFA) may provide an alternative treatment for patients with unresectable colorectal liver metastases (CRLM). Although the results in literature look promising, uncertainty exists with regard to complication risks and survival for this therapy.

Methods: From January 2000 to May 2013, patients were included in a prospective multicenter database when treated for CRLM. Exclusion criteria were: two-staged treatment, synchronous resection of liver metastases and primary tumor, loss to follow-up or extrahepatic metastases. Patients were divided in a resection-only group (ROG) and combination group (CG). Outcome variables were retrospectively analyzed.

Results: In CG, 98 patients were included versus 534 patients in ROG. There were no differences in general patient characteristics. Patients in CG had a higher Fong clinical risk score (CRS; $P = 0.001$), better ASA classification ($P = 0.04$) and received more neoadjuvant chemotherapy ($P = 0.001$). There was no difference in postoperative morbidity or 90-day mortality. The 5-year disease-free survival (DFS) for CG and ROG was 25% and 36.1% ($P = 0.03$), respectively. For the 5-year overall survival (OS) this was respectively 42% and 62.2% ($P = 0.001$). On multivariate analysis, Fong CRS was a significant predictor for DFS. For OS, Fong CRS, ASA class IV and the combination therapy were significant predictors.

Conclusion: The combination of hepatic resection and intraoperative RFA is a safe procedure, without increase in postoperative morbidity or mortality. Combining RFA and resection in one session is a valid treatment option for patients who would otherwise be inoperable.

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Keywords: Colorectal neoplasms; Liver; Radiofrequency catheter ablation; Hepatectomy

Abbreviations: CRLM, colorectal liver metastases; RFA, radiofrequency ablation; ROG, resection-only group; CG, combination group; CE-CT, contrast enhanced computed tomography; PET-CT, positron emission tomography CT; CUSA, Cavitron Ultrasonic Surgical Aspirator.

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Introduction

Colorectal carcinoma is one of the most commonly diagnosed malignancies, currently listed as third and second diagnosed cancer for respectively males and females in developed countries.^{1,2} The liver is the dominant site for colorectal metastatic disease,³ which develop either metachronous or synchronous in up to 50% of patients.^{4–6} For curative treatment of colorectal liver metastasis (CRLM), hepatic resection is considered the treatment of choice. Patients with CRLM can only be operated with curative intent in approximately 10–25% of cases.⁷ Unfortunately, the majority of patients are ineligible for surgery, because they have unresectable tumors according to several criteria for resectability, such as lack of reserve liver parenchyma, ill location of metastasis near vital structures or presence of extrahepatic disease. In order to provide therapy for these patients, several multimodality treatment options in combination with resection are available, such as neo-adjuvant chemotherapy, two-staged liver resection, portal embolization and alternative therapies.^{8–11} Cryosurgery, microwave ablation and radiofrequency ablation (RFA) are examples of ablative techniques of which RFA is one of the most researched, which uses high-frequency electromagnetic waves to induce localized thermal coagulative necrosis.^{12–16}

Although RFA, as a singular treatment, is shown to be inferior to hepatic resection for the treatment of metastases larger than 3 cm, this therapy is still a viable treatment for smaller lesions.^{17,18} By combining hepatic resection with RFA, patients can be treated for multiple colorectal metastases by resecting larger tumors and, in the same session, ablate smaller lesions with RFA, providing possible cure for patients who previously could not have been treated with resection alone. However, since RFA induces a necrotic area during surgery, the combination of RFA and resection in one session could increase the rate of postoperative complications.

The goal of this study was to compare hepatic resection with or without neo-adjuvant chemotherapy in combination with RFA to conventional hepatic resection with regard to complications, disease-free survival and overall survival.

Materials and methods

Patients

Data concerning patients treated for CRLM were recorded in a multicenter database from two tertiary hospitals (Erasmus MC Cancer Institute, Rotterdam, The Netherlands; Radboudumc, Nijmegen, The Netherlands) and retrospectively analyzed. IRB approval was not necessary as participating hospitals issued a waiver of consent. Data was collected concerning patient demographics, pre- and post-operative results and operation details.

From January 2000 to May 2013, 1007 patients were included in this database. Patients were deemed eligible for inclusion when they received either partial hepatic

resection or a combination of both RFA and resection in one session for the curative treatment of CRLM. This included patients with newly found metastases by a radiologist on intraoperative ultrasound (IOUS), subsequently treated with RFA. Patients presenting with recurrent CRLM after previous resection were excluded. Other exclusion criteria were: evidence for extrahepatic disease ($n = 96$), missing follow-up data ($n = 111$), those operated with a two staged approach ($n = 56$), patients treated with only RFA ($n = 27$) or patients who received synchronous resection for both colorectal primary and metastases ($n = 85$), leaving a total of 632 included patients. Patients were then divided in two groups: a resection-only group (ROG) and a combination group (CG).

Medical history was documented and baseline physical examination with serum laboratory tests were fulfilled. Patients additionally received an abdominal contrast enhanced computed tomography (CE-CT) and an additional full body positron emission tomography in combination with CT (PET-CT) in case of suspected extrahepatic disease, depending on the multidisciplinary tumor board decision. Patients were categorized according to clinical risk score as described by Fong et al.¹⁹ Prior to treatment, all patients were discussed in multidisciplinary tumor boards.

Perioperative chemotherapy is not considered the standard of care in all patients with primarily resectable CRLM in the participating hospitals. The patients who received neoadjuvant chemotherapy, showed metastases which were initially unresectable or difficult to resect due to either an adverse location, proximity to vascular/biliary structures or presented with multiple (≥ 4) CRLM. A proportion of patients in this study already received neoadjuvant systemic therapy in referring hospitals according to local protocols. Chemotherapy consisted of a combination of 5-fluorouracil/capecitabine and oxaliplatin/irinotecan with or without bevacizumab. Tumor response was assessed after 2/3 cycles with the use of CE-CT, according to the RECIST criteria,²⁰ and CEA levels. Further treatment was considered depending on the response of disease. If deemed resectable, surgery was planned approximately 3–4 weeks after the last course of chemotherapy. Bevacizumab needed to be excluded for 6 weeks before surgery. A minority of patients received adjuvant chemotherapy as part of a study protocol in the Netherlands.²¹

Hepatectomy

Surgery was performed, using an open approach and the abdominal cavity was explored to confirm the absence of extrahepatic disease. The liver was examined by the surgeon and a radiologist was present to perform an intraoperative ultrasound to identify the number and location of lesions. Minor or major hepatic surgery was performed depending on size, number and location of the liver lesions. The Cavitron Ultrasonic Surgical Aspirator (CUSA) was in both centers the preferred instrument for dissecting the

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