



A multiple microwave ablation strategy in patients with initially unresectable colorectal cancer liver metastases – A safety and feasibility study of a new concept

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Abstract

Aims: Resection for colorectal cancer liver metastases is indicated when an R0 resection with preservation of a sufficient future liver remnant (FLR) is achievable. Multimodality conversion of initially unresectable patients to resectable is possible in some patients. We present results of a downstaging strategy using microwave ablation (MWA).

Patients and methods: In patients where resection was precluded by absence of a tumour-free FLR due to the extent of segmental tumour engagement, but with the potential to clear the whole liver with multiple local ablations, MWA was performed at laparotomy using ultrasound guidance or computer-assisted navigation. Mortality and morbidity was recorded and the overall and disease-free survival of the ablated patients was compared to data of two historic cohorts.

Results: Ten of twenty treated patients were alive at median follow-up 25 months. There was no perioperative mortality, with MWA-associated complications being mild to moderate. The MWA group showed a 4-year overall survival of 41%, compared to 70% for a historic cohort of primarily resected patients and 4% for patients with palliative treatment.

Conclusion: Results of the multiple ablation strategy in the defined population suggest a survival benefit, compared to palliative chemotherapy alone with acceptable associated morbidity and no perioperative mortality.

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Introduction

Colorectal cancer (CRC) is the third leading cause of cancer death in the world and among the leading causes of tumour-associated deaths in Western countries.¹ Twenty-five to fifty percent of patients with CRC have liver metastases, either detected at diagnosis of the primary tumour (synchronous) or at a later stage (metachronous).^{2–4} The criteria for curative-intended surgery of colorectal cancer liver metastases (CRCLM) have changed during recent years. Currently, resectability is defined as the ability to

perform a complete (R0) resection for intra- and extrahepatic disease (regardless of the extent of the tumour-free margin), while preserving a sufficient future liver remnant (FLR).⁵ From a surgical point of view, patients with CRCLM can be divided into three groups, namely readily resectable, those that are unresectable at time of diagnosis, but with the potential to downstage or convert to resectable, and those that are initially unresectable and unlikely to ever become resectable.

Thus, with the current resectability paradigm, irresectability is defined as the inability to create a tumour-free FLR because of combinations of the extent of segmental tumour engagement, tumour engagement of structures crucial for functioning of the FLR (arterial and portal supply; biliary and venous drainage) or insufficient volume of the FLR.

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Although LA of liver tumours is not new, recent developments such as the introduction of microwave ablation (MWA) and irreversible electroporation (IRE) as alternatives to radiofrequency ablation (RFA) have offered possible extension of indications, with renewed interest in the concept.^{6,7} MWA has advantages compared to RFA, most importantly, lower susceptibility to the heat-sink effect of large vessels.⁸ These modalities are used with increasing frequency as part of multimodality treatment of patients with CRCLM.^{1,9} For patients with advanced disease who do not meet the resection criteria, addition of LA to palliative chemotherapy may increase survival and quality of life, compared to chemotherapy alone.¹⁰

In this paper we present the concept of multiple MWA, if necessary combined with local resection in patients with CRCLM where the metastatic burden precludes a sufficient post-surgery FLR. The emphasis of the paper is on feasibility and safety, but also survival is reported, comparing the results with historic best-case and worst-case scenario cohorts.

Materials and methods

In Stockholm county patients with confirmed or suspected CRCLM are, after dedicated liver-specific imaging, discussed at an inter-hospital hepatobiliary multidisciplinary treatment (MDT) conference for assessment and treatment planning, with intervention performed in a centralized liver unit. In patients where primary curative-intended treatment is precluded by absence of a tumour-free FLR due to the extent of segmental engagement, a strategy of multiple MWA, with or without local resection, was adopted in selected patients. A prerequisite for the planned intervention was that the whole liver could be rendered macroscopically tumour-free. LA of lesions <35 mm in diameter was performed at laparotomy using MWA (Acculis MTA, Angiodynamics, Latham, NY, USA) with intra-operative ultrasound (US) guidance or computer-assisted (CA) navigation (CAS-ONE, CAScination, Bern, Switzerland).¹¹ Local resection was performed for tumours engaging the liver surface. Pre-operative antibiotic prophylaxis was used in all patients. Chemotherapy was administered as neo-adjuvant, adjuvant (related to the primary cancer operation or liver intervention) or palliative treatment, as recommended by the relevant MDT. All patients were followed up with CT or US 1 month after treatment, every 3 months for 1 year and 6-monthly thereafter. In case of tumour recurrence (local recurrence of previously treated tumours or newly visible metastases), patients were discussed in the MDT conference and if so recommended, suitable cases were re-treated with LA and/or resection.

The outcome of the ablated patients group was compared with the outcomes of two cohorts selected from all patients diagnosed with CRC in Stockholm county in 2008 and followed up for 5 years to identify patients that

develop liver metastases and to determine the outcome of patients that developed liver metastases. The first cohort, representing a best-case scenario, consisted of all patients that were resected. The second cohort, representative of a worst-case scenario, consisted of patients that had undergone palliative oncologic treatment for liver metastases, <85 years of age, having <20 metastases with a maximum size ≤ 30 mm and no unresectable extrahepatic disease.

Statistical analysis

Descriptive statistics were used for presentation of patient characteristics, presented either as medians with minimum and maximum values or as proportions. Differences between groups were analysed using the Mann–Whitney *U*-test or Fisher's exact test as appropriate. Survival curves were calculated using Kaplan–Meier estimates and survivor functions were compared using the log-rank test. Independent predictors of survival were identified and hazard ratios calculated using the Cox proportional hazards model, using both univariate and multivariate regression models. The threshold for statistical significance was set to $\alpha < 0.05$. STATA 10 (StataCorp, College Station, Texas 77845 USA) was used for the statistical analyses.

Results

Between October 2009 and September 2012, twenty patients with multiple CRCLM were treated with the multiple MWA strategy. The control groups consisted of 36 resected and 25 palliatively treated patients selected from 271 patients diagnosed with liver metastases in the 5-year follow-up of 1026 patients presenting with CRC in 2008. Demographic and tumour characteristics of the study group and control groups are summarized in Table 1. Treatment parameters of the MWA group are shown in Table 2. In 12 patients, the MWA was performed at the same time as the primary cancer operation. The median number of ablations was 7 (range 4–22). Navigation was US-guided in 13

Table 1
Patient characteristics.

	MWA <i>n</i> = 20	Resected <i>n</i> = 36	Palliative <i>n</i> = 25	<i>p</i> -Value ^c
Age (years); median (min–max)	64 (44–82)	65 (42–83)	68 (49–83)	<i>p</i> = 0.75
Male/female	9/11	23/13	15/10	<i>p</i> = 0.38
Tumour characteristics				
Synchronous ^a / metachronous detection	18/2	17/19	15/10	<i>p</i> < 0.05
Number; median (min–max)	9 (5–22)	2 (1–15)	5 (1–16)	<i>p</i> < 0.05
Size (mm) ^b ; median (min–max)	27 (10–54)	17 (6–30)	19 (10–28)	<i>p</i> = 0.07

^a Synchronous defined as detected within 90 days of the primary tumour.

^b Size at initial presentation.

^c MWA group vs. palliative group.

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