



Clinical outcomes for patients with liver-limited metastatic colorectal cancer: Arguing the case for specialist hepatobiliary multidisciplinary assessment

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Abstract

In patients with liver-limited metastatic colorectal cancer, hepatic resection can offer a significant survival benefit over systemic therapy alone. Specialist hepatobiliary multidisciplinary meetings are currently believed to provide the best forum to discuss the management for these patients.

A retrospective analysis was undertaken of patients diagnosed with liver-limited metastatic colorectal cancer over 6 months within a cancer network in the United Kingdom. In addition, patients who were diagnosed but not referred to the hepatobiliary meeting were discussed within a virtual multi-disciplinary setting. Contributors were blinded and proposed management recorded.

159 newly diagnosed patients with liver-limited metastatic colorectal cancer were identified. 68 (43%) were referred at initial diagnosis and 38 (24%) referred following systemic treatment. 35 (51%) who were discussed at baseline underwent a subsequent hepatectomy or radiofrequency ablation, as did 18 (47%) patients referred after chemotherapy. Of the remaining 53 (33%) patients not referred, imaging was available for 31 (58%). Decisions regarding potential liver-directed therapy were discussed within a multi-disciplinary setting. 13 (42%) were identified as resectable or potentially resectable and 11 (36%) may have been suitable for a clinical trial. In reality, none of these 31 patients (100%) underwent surgery or ablation.

Whilst the majority of patients with liver-limited metastatic colorectal cancer were referred appropriately, this study demonstrates that a significant number with potentially resectable disease are not being discussed at specialist meetings. A review of all diagnosed cases would ensure that an increased number of patients are offered hepatic resection or ablation.

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Introduction

Colorectal cancer (CRC) is the 3rd leading cause of cancer related mortality worldwide. Advances in systemic therapy have changed the treatment paradigm of stage IV disease and the median overall survival for metastatic CRC is now 26–30 months with 5-year survival rates of 11%.^{1–3} Yet there is mounting evidence demonstrating

improved outcomes in a select group of patients with resectable liver-limited metastases. R0 hepatic resections can lead to 5-year survival rates of 36–58% and 10-year figures can reach 17–26%.^{4–6} In CRC, the liver is often the initial site of metastatic spread due to direct invasion via the hepatic portal vein. 20% of patients with stage IV disease present with CRC liver metastases (CLM) with a further 50% or more developing subsequent metachronous CLM. As several retrospective studies have now demonstrated significantly improved survival following hepatic metastasectomies, it is no longer justifiable to perform randomised trials comparing surgery with systemic treatment alone.^{5–7}

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As expected, an R0 resection is required to achieve optimal survival and thus liver metastasectomy remains a highly skilled procedure. In the United Kingdom (UK) these operations are restricted to specialist hepato-biliary (HPB) units following discussion within a specialist HPB oncology multi-disciplinary meeting (MDM). Each MDM should include dedicated HPB surgeons, radiologists and oncologists. A proposed pan-European consensus suggested that MDM discussions should take place both at presentation and prior to subsequent major treatment decisions.⁸ Current National Institute for Health Care and Excellence (NICE) guidelines state that if a computer tomography scan of a patient with CRC shows metastases confined to the liver, a specialist HPB MDM should decide whether further imaging is needed to confirm whether surgery is possible for the patient (or potentially possible) after further treatment.⁹ NICE guidance also states that local cancer networks should agree pre-determined criteria specifying which patients should be referred to the HPB MDM. However, the definition of what constitutes resectable disease continues to evolve with advancing surgical and imaging techniques and therefore should only be determined by a specialist team. Historically, metastasectomies were reserved for patients with isolated liver lesions. Yet the combination of novel systemic therapies and more sophisticated surgical procedures mean resections can now be offered to patients with more extensive disease. Therefore, many clinicians are now of the opinion that all patients with limited CLM should be referred for specialist HPB MDM review to avoid inappropriately denying patients surgery. Patients not suitable for hepatic resection, but with isolated liver metastases, should be enrolled in clinical trials where possible. Outcomes for loco-regional therapies such as microwave ablation (MA), radiofrequency ablation (RFA), irreversible electroporation or selective internal radiation therapy (SIRT) remain largely undetermined and prospective studies are required to evaluate their benefit.^{10–13} Results from a recently reported phase II study demonstrating improved overall survival in patients with up to 9 CLM treated with combined chemotherapy and RFA compared with chemotherapy alone suggests multi-modality treatment may be of benefit.¹⁴ Further UK guidelines addressing the resection of CLM were proposed by a select panel including liver surgeons, gastroenterologists, oncologists, diagnostic and interventional radiologists and general surgeons in 2006. It stated that patients under consideration of loco-regional treatment to hepatic metastases should be discussed within a specialist HPB MDM. In addition, consideration of patients for resection of liver metastases should be carried out by a high volume centre and the decision regarding fitness for surgery should be undertaken by an anaesthetist and liver surgeon. Despite these guidelines, there appears to be significant discordance within referral practices to specialist HPB MDMs and the subsequent management of liver-limited disease. The rate of CLM resection has been shown to vary significantly across the UK.¹⁵

We conducted a study that retrospectively assessed referral rates for patients with liver-limited metastatic CRC to the central HPB MDM over a 6-month period, within a large dedicated cancer network. Cases that had not been discussed were then referred for virtual HPB MDM discussions with MDM contributors blinded to assess potential disparity between referral rates and suitability for surgery, SIRT or inclusion within a clinical trial.

Methods

A retrospective analysis was undertaken of all patients with liver-limited metastatic CRC across a 6-month period in 2012 within the South East London Cancer Network (SELCN) and Kent and Medway Cancer Network (KMCN). The combined population served by these networks is approximately 2.9 million. All cases diagnosed with CRC within both networks during this time period were collated from local CRC MDM referral data. From these records, all patients with liver-limited CRC were then identified. Using information from a prospectively maintained MDM database from the HPB centre, patients were categorised into three groups; patients referred to the specialist HPB MDM at diagnosis, those only referred following initial treatment and those that were never referred. Each referring hospital had a local CRC MDM that included colorectal surgeons, medical and clinical oncologists and diagnostic radiologists. In these hospitals, one of the specialist HPB surgeons from the tertiary liver centre attended these CRC MDMs monthly. The centre specialist HPB MDT occurred twice weekly and was attended by HPB surgeons, interventional radiologists, colorectal surgeons, histopathologists and medical and clinical oncologists. Information regarding baseline demographics, performance status, disease distribution and management were collated.

For patients that had not been discussed within the specialist HPB MDM, a subsequent virtual MDM discussion with a liver surgeon, a dedicated liver radiologist and an oncologist was organised at the tertiary centre for all cases where imaging was available. Patients were discussed within 'real-life' MDMs and participating MDM contributors were blinded for each discussion. Proposed management was then compared with actual outcomes for each patient.

To compare categorical variables, the chi-squared test or the Fischer's exact test was used where appropriate. To compare continuous variables, the Mann–Whitney (two-tailed) test was used. Statistical analysis was performed using SPSS software package version 22.

Results

159 Patients with liver-limited metastatic colorectal cancer were identified. 68 Patients (42.7%) were referred to the specialist HPB MDM at initial presentation of liver

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