

ORIGINAL ARTICLE

Colorectal liver metastases: disappearing lesions in the era of Eovist hepatobiliary magnetic resonance imaging

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Abstract

Background: Hepatobiliary contrast enhanced MRI is known to be the most sensitive imaging modality for detection of colorectal hepatic metastasis. To date no study has investigated the rate of disappearing lesions with gadoxetic acid MR (Eovist/Primovist), or characterized the pathologic response of lesions which disappear on gadoxetic acid MR.

Methods: Retrospective review of hepatic resections for colorectal metastases between 01/2008 and 01/2014 was performed to evaluate the rate of disappearance of lesions on gadoxetic acid MR and the rate of complete pathologic response in the lesions that disappear. “Disappearing lesions” were lesions on baseline imaging that were not identifiable on pre-operative Eovist MRI. Complete pathologic response was defined as no viable tumor on pathology or by lack of recurrence within 1 year.

Results: In 23 patients, 200 colorectal metastases were identified on baseline imaging. On pre-operative Eovist MR 77 of the 200 lesions (38.5%) were “disappearing” lesions. At surgical pathology or 1 year follow-up imaging, 42 of 77 lesions (55%) demonstrated viable tumor (21) or recurrence (21). Thirty of 77 lesions (39%) were nonviable at pathology (10) or without evidence of recurrence at 1 year (20). 5 lesions were indeterminate.

Discussion: Despite disappearance on Eovist MR imaging (the most sensitive available imaging modality), 38.5% of all colorectal metastases disappeared and of those, 55% were viable.

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Introduction

Colorectal cancer results in an estimated 600,000 deaths per year worldwide, with 1.2 million new cases annually, making it the 3rd most common cancer in men and the 2nd most common cancer in women.¹ Hepatic metastatic disease has been found in 56% of patients with colorectal cancer at autopsy, with isolated hepatic metastases in 35% of patients.² Metastatic colorectal cancer has a poor prognosis with overall 5 year survival of 12–17%.^{3,4} Patients who undergo intent to cure resection for hepatic metastatic disease have demonstrated improved 1 year survival of 93% and 5 year survival of 47%.⁵

Prior to undergoing hepatic resection, patients with hepatic metastatic disease often receive neoadjuvant chemotherapy, which can result in lesions “disappearing” or becoming radiologically occult (Fig. 1). Despite a complete response on imaging, many studies have shown persistent viable tumor at the site of “disappearing lesions”.^{6–12} With a lesion based analysis, the incidence of disappearing lesions ranges from 11%¹² to 36%⁷ of initially detected liver metastases. With a patient based analysis, disappearing lesions have been shown to occur in 6%⁷–23%¹³ of patients treated for colorectal metastatic disease. Reported complete pathologic response of disappearing lesions ranges from 15%¹⁰ to 73%.⁶ While the current surgical dogma mandates removal of all tumor if feasible, the role of disappearing lesions in pre-surgical planning remains controversial with no demonstrated survival benefit to resecting all sites of disappearing lesions.¹⁴

This study was presented at the Annual Meeting of the AHPBA, 11–15 March 2015, Miami, Florida.

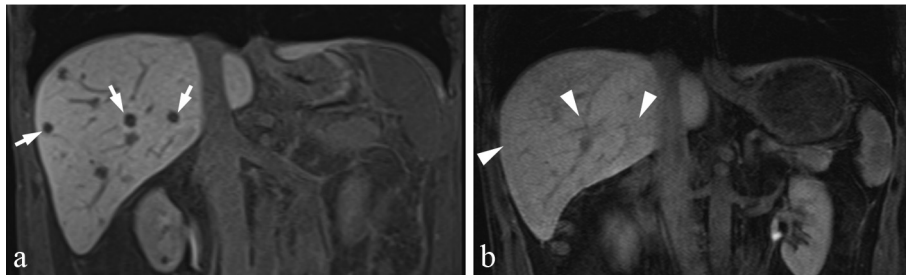


Figure 1 Coronal hepatobiliary 20 min delay MR image at baseline (a) demonstrating colorectal metastases in the liver (arrows). Coronal hepatobiliary 20 min delay MR image at pre-surgical staging (b) demonstrating no lesion at the site of metastases on the prior exam (arrowheads).

Studies investigating disappearing lesions rely on a variety of imaging modalities, including PET/CT, US, contrast enhanced CT, MRI, and intra-operative US. Bischof *et al.* 2013 report a pooled sensitivity for hepatic metastases after chemotherapy of 85.7% for MRI and 69.9% for CT, and suggest MRI is the preferred modality for pre-operative evaluation of hepatic metastases. Over the past 7 years there has been an increasing reliance on a new MRI contrast agent gadoxetic acid (Eovist or Primovist; Bayer Healthcare Pharmaceuticals) for imaging colorectal hepatic metastases. Gadoxetic acid has increased sensitivity over previously available MR techniques,¹⁵ and shows improved sensitivity for small colorectal metastases over CT,¹⁶ especially in the setting of background hepatic steatosis. To date no study has investigated the rate of disappearing lesions with gadoxetic acid MR, or characterized the pathologic response of lesions which disappear on gadoxetic acid MR.

Gadoxetic acid is characterized as a hepatobiliary contrast agent due to its high rate of uptake and excretion by functioning hepatocytes. On 20 min delayed imaging, (often referred to as hepatobiliary phase) gadoxetic acid uptake peaks in normal liver, with liver lesions becoming dark areas of non-enhancement (Fig. 2). The hepatobiliary phase allows for optimal conspicuity of lesions compared to background liver and is the reason for the improved sensitivity for lesion detection with gadoxetic acid compared to other MRI contrast agents.

Ideally, patients with colorectal hepatic metastatic disease receive high quality quadruple phase CT or gadoxetic acid MR prior to undergoing neoadjuvant chemotherapy to serve as a roadmap for hepatic resection. In reality many of patients are

diagnosed and staged at outside institutions, and often receive chemotherapy prior to establishing care at tertiary care centers with experienced hepatobiliary surgeons. With outside imaging as a reference, Eovist MR may be performed prior to resection to assess treatment response and determine the extent of disease.

The purpose of our study was to determine the incidence of disappearing colorectal metastases with state-of-the-art hepatobiliary agent MR imaging and assess the rate of complete pathologic response for disappearing lesions on hepatobiliary phase MR imaging. We hypothesize gadoxetic acid is more sensitive for viable colorectal metastases, and disappearance on gadoxetic acid imaging is more likely an indication of pathologic complete response compared to reported rates of viability on other less sensitive imaging modalities.

Methods

Patients

After IRB approval and waiver of consent, a database of surgery clinic patients was queried using the following ICD 9 codes – 197.7 (Secondary neoplasm of the liver) and 153.* (neoplasm of colon) or 154.0 (neoplasm rectosigmoid junction) or 154.1 (neoplasm rectum). The dates of inclusion were January 1st, 2008 to January 1st, 2014. Patients were then cross referenced to a database containing all patients imaged with gadoxetic acid at our institution. The individual medical records were then reviewed to determine eligibility based on the following inclusion criteria: diagnosis of colorectal cancer, evidence of metastatic colorectal cancer, treatment of colorectal metastatic disease with liver resection, pre-operative re-staging with

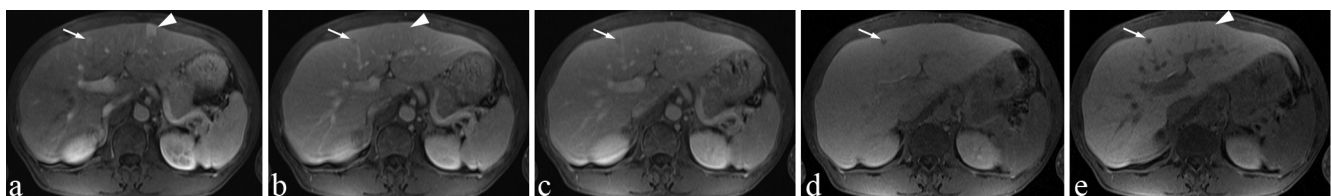


Figure 2 Arterial phase: hepatic artery and early portal vein enhancement (A). Portal Phase: peak portal vein enhancement (B). Transitional phase: early parenchymal uptake (C). Transitional 5 min phase: gradual blood pool clearance (D). Hepatobiliary 20 min phase: blood pool clearance with peak normal liver parenchymal enhancement. Note the colorectal metastasis (arrow) and the arterial shunting (arrowhead).

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