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#### **ORIGINAL ARTICLE**

# Is intraoperative ultrasound still useful for the detection of colorectal cancer liver metastases?

Guillaume Hoch<sup>1</sup>, Valérie Croise-Laurent <sup>2</sup>, Adeline Germain<sup>1</sup>, Laurent Brunaud<sup>1</sup>, Laurent Bresler<sup>1</sup> & Ahmet Ayav<sup>1</sup>

1 Departments of Hepatopancreatobiliary Surgery, and 2 Radiology, Nancy-Brabois Hospital, Faculty of Medicine, University of Nancy, Nancy, France

#### **Abstract**

**Background:** Debate on the optimal mode of preoperative imaging in the management of colorectal liver metastases (CRLM) is ongoing and, despite its longstanding use, the precise role of intraoperative ultrasonography (IOUS) is not well established. This study evaluates the impact of IOUS in the era of high-quality, cross-sectional imaging techniques.

**Methods:** All patients who underwent liver resection for CRLM in a tertiary care referral centre from January 2006 to December 2013 were included. All patients were submitted to computed tomography (CT) and/or liver magnetic resonance imaging (MRI) before surgery. Intraoperative US was performed mainly to detect previously non-diagnosed tumours that would change the surgical strategy.

**Results:** A total of 225 liver resections were performed. Liver MRI and CT scans were available for 202 patients (89.8%) and 225 patients (100%), respectively. Radiological reports recorded 632 liver tumours in 219 patients (i.e. 2.9 lesions per patient). The median time between preoperative liver MRI and surgical resection was 36 days. Intraoperative inspection, palpation and US found 20 additional lesions in 18 patients (8.0%), in three of whom lesions were diagnosed only on IOUS (1.4%). Overall, only 12 of the 20 lesions were malignant.

**Conclusions:** Although CT and liver MRI are commonly used, IOUS alone allows the discovery of a few additional lesions that result in a change of surgical strategy in 1.4% of cases.

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#### Correspondence

Ahmet Ayav, Department of Hepatopancreatobiliary Surgery, Hôpitaux de Brabois, Allées du Morvan, 54505 Vandoeuvre-les-Nancy, France. Tel: + 33 3 83 15 31 20. Fax: + 33 3 83 15 31 19. E-mail: a.ayav@chu-nancy.fr

#### Introduction

Over 42 000 cases of colorectal cancer are diagnosed every year in France. The disease is one of the most common causes of cancer-related death and involves the second most frequent location of cancer in both sexes. Liver metastases from colorectal primary tumours are observed at diagnosis in 20% of patients<sup>2</sup> and in 50–75% of patients within 3 years. <sup>3,4</sup>

The liver is the most common site of colorectal cancer metastasis, the occurrence of which represents the most critical prognostic factor as colorectal liver metastases (CRLM) are the main cause of mortality in two-thirds of cases.<sup>5</sup> Margin-free (R0) surgical resection is the goal and leads to 5-year survival rates of around 40% and 10-year survival rates can reach 25%, with low mortality (<1%) and morbidity (20–40%) rates in high-volume centres.<sup>6–9</sup>

Intraoperative ultrasonography (IOUS) is widely used by surgeons, but its results are conflicting. Systematic IOUS liver

examination has been shown to yield significant new information and may identify at least one additional lesion not seen on preoperative imaging in 10–26% of patients and change the surgical strategy in up to 72% of patients.<sup>5,10–12</sup> However, in most of the series reported to date, preoperative assessment is variable and does not include systematic preoperative computed tomography (CT) or liver magnetic resonance imaging (MRI).

Liver MRI is used before surgery by some authors, who argue that its sensitivity in the detection of liver metastases is about 90%. Others advocate the use of preoperative fluorodesoxyglucose positron emission tomography (FDG-PET) or CT screening before surgery. 12,13

The present study was conducted to assess the role of IOUS in the management of liver metastasis from colorectal cancer, in an era marked by the frequent use of high-quality, cross-sectional imaging techniques.

#### **Materials and methods**

#### Study population

This single-centre study included all patients who underwent liver resection for CRLM from January 2006 to December 2013 at Nancy-Brabois University Hospital.

Data were collected from the tertiary referral centre database. Clinical, pathological and radiological parameters and outcomes were analysed. These included age at diagnosis and at surgery, gender, body mass index (BMI), American Society of Anesthesiologists (ASA) score, primary tumour location and the date of primary tumour resection. Data on any history of preoperative or postoperative chemotherapy were also collected. All radiology reports from liver MRI and CT scans were reviewed. Intraoperative information, such as liver IOUS scan details, type of resection and operative time, and postoperative morbidity and mortality were recorded.

All patients had a histologically confirmed primary colorectal cancer, resected or in place. Synchronous or metachronous (i.e. >6 months after the identification of colorectal cancer) liver metastases were diagnosed using CT and/or liver MRI and/or FDG-PET.

All patients were discussed in a multidisciplinary team (MDT) meeting, which included a radiologist specializing in liver disease, hepatopancreatobiliary (HPB) surgeons and an oncologist, to confirm the indications for surgery and/or chemo therapy and/or radiotherapy.

#### Preoperative imaging

All patients underwent CT and/or liver MRI before surgery. Scanning by FDG-PET was not routinely performed. Liver MRI studies were carried out using a 1.5-T superconducting system (Signa Excite HDx; General Electric Healthcare, Milwaukee, WI, USA) with three axial sequences: fast spin echo T2 (FSET2-1.5T); single-shot diffusion-weighted echoplanar imaging (DWI-1.5T), and an in- and out-of- phase T1 weighted sequence. Three-dimensional liver acquisition with volume acceleration sequences (LAVA) after gadoteric acid injection (Dotarem<sup>®</sup>; Laboratoire Guerbet, Aulnay-sous-Bois, France) were also performed.

#### Intraoperative staging

Abdominal exploration was achieved first by visual inspection and bimanual palpation, except in the laparoscopy group. The liver was fully mobilized to facilitate US exploration of the organ. Intraoperative US was performed by an experienced hepatobiliary surgeon (AA, LBre) or by an experienced radiologist (VC-L). Intraoperative US was performed to detect previously non-diagnosed tumours that would change the surgical strategy, and also to guide liver resection by localizing the Glissonian structures and hepatic veins. Intraoperative US did not focus on liver parenchyma that was scheduled for resection, but concentrated only on the intended residual liver. During these procedures, only new

lesions were counted; previously known lesions were not systematically counted.

#### Follow-up

Postoperative treatments were assessed at the MDT meeting. Thoracic and abdominal contrast-enhanced helical CT scans were performed every 3 months for 2 years. This work-up was complemented with liver MRI if necessary.

#### Data analysis

Statistical analysis was performed using R for Windows Version 3.0.2 (R Foundation for Statistical Computing, Vienna, Austria). Results were expressed as either the median (range) or the mean  $\pm$  standard deviation (SD). Differences in means between groups were compared using the Wilcoxon test. Comparisons between categorical variables were analysed using Fisher's exact test. *P*-values of <0.05 were considered to indicate statistical significance.

#### **Results**

#### Demographic and clinical characteristics

A total of 225 liver resections were performed during the study period. Demographic data are provided in Table 1. Liver metastases were metachronous in 106 patients (47.1%). The median time between primary and CRLM resection was 17.6 months (range: 6.1–73.0 months). In the synchronous group (n = 119), 19 patients (16.0%) were submitted to surgery based on a liver-first strategy, 20 patients (16.8%) underwent the resection of both the primary tumour and all liver metastases during the same operative procedure, and 80 patients (67.2%) underwent a colorectal resection first. In the latter subgroup (n = 80), colorectal cancer resection was performed first in 21 patients (26.3%) because of emergency [intestinal obstruction (n = 15), perforation (n = 1) and abdominal pain (n = 5)]. Thirteen patients (16.3%) underwent two-stage liver resection including primary tumour resection and clearance of the liver left lobe. In 12 patients (15.0%) liver metastases was diagnosed within 6 months of the primary malignancy resection, and 34 patients (42.5%) were referred to the present tertiary referral centre after colorectal tumour surgery.

Overall, repeat hepatectomy was performed in 32 cases (14.2%). One patient underwent three resections.

## Therapeutic modalities of liver metastases

#### Preoperative chemotherapy

A total of 145 patients (64.4%) underwent preoperative chemotherapy. Sixty patients (41.4%) had resectable disease and were treated using the FOLFOX 4 protocol as described by the European Organization for Research and Treatment of Cancer (EORTC).<sup>14</sup> A total of 85 patients (58.6%) were identified as having potentially resectable liver metastases and underwent induction chemotherapy, with antiangiogenic or targeted therapies. A mean of 7.4 cycles of preoperative chemotherapy

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