The value of intraoperative ultrasound and preoperative imaging, individually and in combination, in liver resection for metastatic colorectal cancer

Jeffrey T Lordan, Katherine M Stenson, Nariman D Karanjia

Royal Surrey County Hospital, Guildford, UK

ABSTRACT

INTRODUCTION Liver resection is proved to offer potential long-term survival for colorectal liver metastases (CRLM). Accurate radiological assessment is vital to enable an appropriate surgical approach. The role of intraoperative ultrasound (IOUS) has been controversial. This study was designed to analyse the accuracy of IOUS compared with that of preoperative imaging (POI) in these patients.

MATERIALS AND METHODS A prospective analysis of 51 consecutive patients who underwent liver resection for CRLM was undertaken. The accuracy of POI and IOUS were correlated and compared with histopathological analysis. Statistical analyses included t-tests, to compare continuous variables, and chi-square and Fisher's exact tests to compare categorical variables. $p < 0.05$ was considered significant

RESULTS POI correlated with histology in 35 patients (68.6%). The sensitivity and specificity were 82.4% and 86.3% respectively. IOUS correlated with histology in 31 (60.8%) patients. The sensitivity and specificity were 84.3% and 76.5% respectively. There was no difference in accuracy between modalities. The accuracy of POI combined with IOUS correlated with histology in 40 patients (78.4%). The sensitivity and specificity were 88.2% and 84.3% respectively. The accuracy of combined modalities was significantly greater than IOUS or POI alone.

CONCLUSIONS POI combined with IOUS may significantly increase the diagnostic accuracy of patients undergoing liver resection for CRLM.

KEYWORDS

Intraoperative ultrasound – Liver surgery – Metastatic colorectal cancer – Magnetic resonance imaging

Accepted 18 February 2011

CORRESPONDENCE TO

Jeffrey T Lordan, Royal Surrey County Hospital, Egerton Road, Guildford, Surrey GU2 7XX, UK
T: +44 (0)1483 571 122; E: dr_lordan@yahoo.co.uk

The incidence of colorectal carcinoma has been steadily increasing in the Western world, with approximately 50% of patients developing metastatic disease.^{1–4} To date, liver resection is the only modality that can offer potential long-term survival.^{1–4} As such, accurate and precise assessment of liver metastases is vital to enable an appropriate surgical approach.^{5,6}

Historically, preoperative imaging (POI) of the liver has been achieved by ultrasound, computed tomography (CT) and magnetic resonance imaging (MRI) with fluorine-18 fluorodeoxyglucose positron emission tomography (FDG-PET) being reserved to detect distant occult metastases.^{5,6} Intraoperative ultrasound (IOUS) is also used routinely in many liver units.

This study was designed to assess the accuracy of POI

and IOUS in patients undergoing liver resection for colorectal liver metastases (CRLM).

Materials and Methods

This was a prospective analysis of 51 consecutive patients who underwent liver resection for CRLM in a single hepatopancreatobiliary (HPB) unit during 2007. All patients underwent preoperative contrast-enhanced CT of the thorax, abdomen and pelvis, and MRI of the liver using intravenous mangafodipir. The POI was analysed by a single dedicated HPB radiology consultant. All patients also underwent IOUS. Preoperative FDG-PET was reserved for selected patients. All liver resections and IOUS were undertaken by the lead surgeon (NDK), who

had more than ten years' experience with IOUS. Liver specimens were then analysed by a dedicated HPB histopathologist.

Patients' demographics, intraoperative blood loss, intra- and postoperative complications, hospital stay and histology (including resection margins and tumour size) were recorded. Complications were categorised according to the classification proposed by Dindo *et al*⁷ and were considered to be severe if they were grade 3 or greater. Postoperative mortality was defined as death within hospital or within 30 days.

Liver parenchyma transection was achieved using a Cavitron® ultrasonic surgical aspirator (Cavitron Corporation, New York, US). Haemostasis was achieved by a combination of the argon beam coagulator, sutures and ligatures, and vascular staplers, where appropriate. During the intraoperative period, the patients' central venous pressure was reduced using anaesthetic techniques.

Statistical analyses included t-tests, to compare continuous variables, and chi-square and Fisher's exact tests to compare categorical variables. These were carried out using SPSS® v15 (SPSS Inc, Chicago, Illinois, US). A *p*-value of <0.05 was considered significant.

Results

Fifty-one consecutive patients who underwent liver resection for CRLM were included in the study. Table 1 shows the patients' demographics and early outcomes. The median age was 66 years, the median intraoperative blood loss was 325ml and the median maximum tumour size was 23mm. The median tumour number diagnosed histologically was 2 (range: 1–18). Two patients required intra- or postoperative blood transfusions and 12 patients underwent intermittent intraoperative Pringle clamping.

Eight patients had perioperative complications, one of which was considered severe according to the scoring

Table 1 Patients' demographics

Patients (n=51)	
Median age (range)	66 years (30.0–84.6)
Male to female ratio	1.2:1
ASA grade:	
1	2%
2	40%
3	7%
Not recorded	2%
Type of liver resection:	
Hemi- or extended hemihepatectomy	25
Parenchymal sparing resection	26
Median intraoperative blood loss (range)	325ml (50–2,000)
Median hospital stay (range)	8 days (3–18)
Morbidity	8 (16%)
Serious complications (≥ ASA grade 3) ⁷	1 (2%)
Mortality	1 (2%)
Number of patients who required blood transfusions	2 (4%)
Use of intraoperative Pringle manoeuvre	12 (24%)
Median maximum tumour size (range)	23mm (1–169)

ASA = American Society of Anesthesiologists

Table 2 Correlation between histological diagnosis, preoperative imaging (POI) and intraoperative ultrasound (IOUS)

Number of tumours	True CRLM diagnosed by histology	Number of patients reported by POI		IOUS		Pre-operative imaging and intra-operative ultrasound combined	
		Overestimated compared with histology	Underestimated compared with histology	Overestimated compared with histology	Underestimated compared with histology	Overestimated compared with histology	Under-estimated Compared with Histology
1	23	2 (9%)	0	2 (9%)	0	1 (4%)	0
2–4	20	4 (20%)	4 (20%)	10 (50%)	2 (9%)	3 (15%)	1 (5%)
5–9	6	2 (33%)	3 (50%)	0	4 (66%)	2 (33%)	2 (33%)
≥10	2	0	2 (100%)	0	2 (100%)	0	2 (100%)

CRLM = colorectal liver metastases

Table 3 Correlation of diagnosis between preoperative imaging (POI) and intraoperative ultrasound (IOUS)

Number of tumours	Number of patients reported by POI	IOUS	
		Overestimated compared with POI	Underestimated compared with POI
1	25	4 (16%)	0
2–4	22	11 (50%)	4 (18%)
5–9	4	0	3 (75%)
≥10	0	0	0

system described by Dindo *et al.*⁷ One patient died in the perioperative period.

POI correlated with histological diagnosis in 35 patients (68.6%). Compared with histological examination, POI overestimated the number of tumours in 7 patients (13.7%) and underestimated it in 9 (17.6%) (Table 2).

The sensitivity and specificity of POI to detect CRLM were 82.4% and 86.3% respectively. However, there was a clear trend of poorer accuracy as the number of true tumours increased.

IOUS correlated with the number of tumours determined by histology in 31 patients (60.8%). IOUS overestimated the number of tumours in 12 patients (23.5%) and underestimated it in 8 (15.7%), compared with histological diagnosis. The sensitivity and specificity of IOUS to detect CRLM were 84.3% and 76.5% respectively.

Diagnoses of CRLM made by POI correlated with IOUS in 29 patients (56.9%). IOUS overestimated the number of tumours within the liver in 15 patients (29.4%) and underestimated it in 7 (13.7%), compared with POI. There was a similar trend towards poorer accuracy as the number of true tumours increased (Table 3).

The combined modalities of POI and IOUS were analysed. The combined modalities correlated with the final histological diagnosis of true CRLM in 40 patients (78.4%). Both modalities overestimated the number of tumours in three patients (5.9%) and underestimated it in five (9.8%). In three patients, the histological tumour number was simultaneously overestimated and underestimated by the two modalities. The sensitivity and specificity of the combined modalities were 88.2% and 84.3% respectively.

Using the two modalities combined was significantly more accurate than using IOUS alone (χ^2 , $p=0.001$; odds ratio [OR]: 0.25, 95% confidence interval [CI]: 0.13–0.40; Fisher's exact test, $p=0.001$) or POI alone (χ^2 , $p=0.001$; OR: 0.15; 95% CI: 0.06–0.28; Fisher's exact test, $p=0.001$).

Discussion

The proportion of patients with CRLM who are eligible for liver resection has steadily increased over the years.⁸ The treatment strategy is an individual approach combin-

ing adjuvant and neoadjuvant chemotherapy, surgery and ablation techniques.^{1,8} Accurate diagnosis of number, size and location of liver lesions is therefore vital. Especially in patients with cholestasis or cirrhosis, who may have limited functioning parenchyma.

The value of IOUS to find metastases undetected by POI and potentially alter intraoperative strategy has been described.^{5,9–12} However, some earlier studies reported a limited clinical value of IOUS.^{13,14} Regarding detection of liver lesions, POI alone attains a sensitivity of 41–68% with transabdominal ultrasound, 60–75% with contrast-enhanced CT and 80–85% with MRI.^{5,5} It is therefore clear to see that a proportion of patients may potentially attend theatre with an inaccurate preoperative diagnosis.

Studies have described the sensitivity of IOUS for detecting liver lesions greater than 10mm as 90–96%.^{5,15} However, this potential accuracy is directly related to the experience of the user. In the current study, the accuracy did not achieve this level despite the experience of the user being greater than ten years. Nevertheless, this may be a reflection of the relatively low number of patients included in the study.

Our study showed that as the number of liver lesions increased, the accuracy of both pre- and intraoperative imaging decreased substantially. However, there was a significant increase in accuracy of information from combined pre- and intraoperative imaging versus each individual modality when compared with the final histology.

Studies have shown that the accuracy of POI drops with liver lesions smaller than 1.5cm.^{5,16} In addition, MRI has particular shortcomings that may contraindicate its use, such as the presence of metal prostheses and claustrophobia.^{5,10} This may explain reports that IOUS detects lesions in up to 40% of patients not detected by POI and alters surgical strategy in 25.7% of patients undergoing resection for CRLM.^{5,16}

The role of IOUS may be more important as laparoscopic liver surgery becomes more frequent due to the absence of intraoperative digital palpation.⁵ In a multicentre European survey that included 37 patients, laparoscopic IOUS was shown to improve the rate of clear resection margins.¹⁷

Although a single experienced HPB surgeon undertook

the IOUS and a single dedicated HPB radiologist interpreted the POI, intra-observer variation and, in particular, MRI performance between units must be considered when interpreting these data. This and the variation of volume of HPB cases between units, means these data may only apply to our unit.

Conclusions

Our study has shown that preoperative CT and MRI in combination with IOUS may significantly increase the diagnostic accuracy of patients undergoing liver resection for CRLM, compared with each individual modality alone.

References

1. Karanjia ND, Lordan JT, Fawcett WJ *et al.* Survival and recurrence after neo-adjuvant chemotherapy and liver resection for colorectal metastases: a ten year study. *Eur J Surg Oncol* 2009; **35**: 838–843.
2. Karanjia ND, Lordan JT, Quiney N *et al.* A comparison of right and extended right hepatectomy with all other hepatic resections for colorectal liver metastases: a ten-year study. *Eur J Surg Oncol* 2009; **35**: 65–70.
3. Kulig J, Popiela T, Klek S *et al.* Intraoperative ultrasonography in detecting and assessment of colorectal liver metastases. *Scand J Surg* 2007; **96**: 51–55.
4. Lordan JT, Karanjia ND. 'Close shave' in liver resection for colorectal liver metastases. *Eur J Surg Oncol* 2010; **36**: 47–51.
5. Piccolboni D, Ciccone F, Settembre A, Corcione F. Liver resection with intraoperative and laparoscopic ultrasound: report of 32 cases. *Surg Endosc* 2008; **22**: 1,421–1,426.
6. DeOliveira ML, Pawlik TM, Gleisner AL *et al.* Echogenic appearance of colorectal liver metastases on intraoperative ultrasonography is associated with survival after hepatic resection. *J Gastrointest Surg* 2007; **11**: 970–976.
7. Dindo A, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann Surg* 2004; **240**: 205–213.
8. Lordan JT, Karanjia ND, Quiney N *et al.* A 10-year study of outcome following hepatic resection for colorectal liver metastases – The effect of evaluation in a multidisciplinary team setting. *Eur J Surg Oncol* 2009; **35**: 302–306.
9. Patel NA, Roh MS. Utility of intraoperative liver ultrasound. *Surg Clin North Am* 2004; **84**: 513–524.
10. Zacherl J, Scheuba C, Imhof M *et al.* Current value of intraoperative sonography during surgery for hepatic neoplasms. *World J Surg* 2002; **26**: 550–554.
11. Mazzoni G, Napoli A, Mandetta S *et al.* Intra-operative ultrasound for detection of liver metastases from colorectal cancer. *Liver Int* 2008; **28**: 88–94.
12. Ong KO, Leen E. Radiological staging of colorectal liver metastases. *Surg Oncol* 2007; **16**: 7–14.
13. Stone MD, Kane R, Bothe A Jr *et al.* Intraoperative ultrasound imaging of the liver at the time of colorectal cancer resection. *Arch Surg* 1994; **129**: 431–435.
14. Flati G, Flati D, Porowska B *et al.* Is intraoperative ultrasonography useful in pancreatic cancer surgery? *G Chir* 1994; **15**: 313–316.
15. Paulson EK. Evaluation of the liver for metastatic disease. *Semin Liver Dis* 2001; **21**: 225–236.
16. Sahani DV, Kalva SP. Imaging the liver. *Oncologist* 2004; **9**: 385–397.
17. Gigot JF, Glineur D, Santiago Azagra J *et al.* Laparoscopic liver resection for malignant liver tumors: preliminary results of a multicenter European study. *Ann Surg* 2002; **236**: 90–97.