

Laparoscopic staging in selected patients with colorectal liver metastases as a prelude to liver resection

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Abstract

Background: Careful selection of patients with colorectal liver metastases for liver resection should minimize the risk of unnecessary laparotomy due to unresectable disease. The impact of staging laparoscopy with laparoscopic ultrasonography (LapUS) on clinical decision making in selected patients with potentially resectable colorectal liver metastases was evaluated. **Patients and methods:** Staging laparoscopy with or without LapUS was performed in 77 of 415 consecutive patients (19%) with colorectal liver metastases deemed potentially resectable following liver-specific CT and/or MRI scanning. Retrospective analysis of prospectively collected data compared clinical outcomes with those in whom laparoscopy had been deferred in favour of laparotomy. **Results:** Staging laparoscopy was successful in 76 of 77 patients (99%). Adverse events occurred in three patients (4%): bowel injury $n=2$; late port site metastasis, $n=1$. Laparoscopic staging identified factors precluding curative resection in 16 patients (21%), thus averting unnecessary laparotomy. Of the 57 patients (74%) staged laparoscopically who underwent surgical exploration, 7 patients (12%) were unresectable and liver resection was achieved in 50 (88%). **Discussion:** Laparoscopic staging remains useful in detecting occult intra- and extra-hepatic tumour in selected patients with potentially operable colorectal liver metastases.

Key Words: colorectal liver metastases, staging laparoscopy, laparoscopic ultrasonography

Introduction

Hepatic resection offers the best chance of cure for patients with colorectal liver metastases [1,2]. As less than one-quarter of all patients presenting with colorectal liver metastases are suitable for liver resection with curative intent, the successful identification of those with resectable disease for operative intervention remains a fundamental goal. Conversely, understaging of the tumour may result in the abandonment of the operation to the detriment of the patient. Despite advances in cross-sectional imaging techniques during the last decade, there has been concern regarding the incidence of non-therapeutic laparotomy [3], and this has stimulated interest in the role of staging laparoscopy (with or without laparoscopic ultrasonography, LapUS) in an attempt to detect previously unsuspected intra- or extra-hepatic disease [4–11].

However, the need to perform routine staging laparoscopy in all patients with potentially operable colorectal liver metastases has been questioned in favour of a more selective approach [8,9,11]. In this way, the reservation of laparoscopy for selected high-risk patients may increase the diagnostic yield and

justify the inconvenience, cost and potential morbidity inherent in the technique.

This study evaluated the impact of selective staging laparoscopy (with LapUS) on the management of patients with colorectal liver metastases in the context of a specialist hepatobiliary unit with a high volume liver resection practice.

Patients and methods

The study comprised 415 consecutive patients with colorectal liver metastases referred during a 4-year period (1 January 2000 to 31 December 2003). Patients were identified from a prospectively maintained computer database comprising 147 data fields.

In all, 77 of 415 patients underwent staging laparoscopy (19%) and their case notes were reviewed retrospectively for further information regarding operation details and clinical decision making ('laparoscopy group'). All had been considered potential candidates for hepatic resection with curative intent on the basis of preoperative cross-sectional imaging.

Criteria for operability required the potential for complete resection of all liver metastases, regardless of

size, number, distribution or width of resection margin. In addition, a sufficient volume of viable liver parenchyma (at least 25% of normal parenchymal volume as estimated from CT and/or MRI) must be preserved. Patients who had favourable preliminary abdominal CT and/or MRI scans, usually performed at the referring institution, were considered for liver resection. Repeat staging investigations at North Hampshire Hospital were performed following referral and comprised both CT arteriportography (CTAP) and MRI in 5 patients, CTAP alone in 28 patients and MRI only in 44 patients. Patient selection for liver resection was based on these secondary imaging investigations.

The technique of CTAP has been described previously in detail [12]. During the latter part of the study from October 2001 onwards, all patients were assessed by MRI scanning according to a standardized protocol using a 1.5 T Siemens Symphony magnet with phased array body coil (Siemens AG, Munich, Germany). All scans were performed during suspended respiration in the axial plane. The following sequences were used: T1 weighted in and opposed phase chemical shift imaging (8 mm slice thickness), T2 HASTE (6 mm slice thickness) and TRUE FISP (10 mm slice thickness). An axial fat saturated T1 weighted volume acquisition (VIBE) (2 mm slice thickness) was acquired prior to intravenous contrast administration. The choice of contrast agent varied but routinely included gadolinium (Omniscan™; gadodiamide, Amersham Health AS, Oslo, Norway) and/or a liver-specific agent (usually Resovist®; Schering AG, Baar, Switzerland). Scans were acquired in the arterial, portal venous and equilibrium phases using the VIBE sequence following the administration of intravenous contrast. All post-contrast volume acquisitions were reviewed on a 3D workstation.

Patients referred with colorectal liver metastases and an unfavourable or indeterminate pattern of disease were subjected to a 'test of time' for 3–6 months. During this time further sequential imaging investigations were performed.

Patients were selected for laparoscopic staging according to the presence of one or more of the following criteria:

- Unfavourable primary tumour status where there were concerns regarding the risk of locoregional recurrence. Specifically, these included those patients with pT4 stage or circumferential resection margin involvement on histopathology, and/or perforation and/or acute obstruction at the index operation.
- Multiple bilobar metastases where there was concern regarding the feasibility or safety of liver resection and where radiological imaging had been regarded as indeterminate.
- Hepatic parenchymal assessment where there was concern regarding the magnitude of the planned liver resection and, specifically, the quantity and/or quality of the liver remnant.
- In addition to the above, where there were concerns regarding medical co-morbidity and the fitness of the patient for major resectional surgery under prolonged general anaesthesia, laparoscopic staging also served as a 'test of anaesthesia'.

Staging laparoscopy with LapUS was performed as a separate procedure from the planned liver resection under general anaesthesia with full muscle relaxation. All laparoscopic procedures were performed or supervised by a single operator (T.G.J.) using a systematic approach, which has been described in detail elsewhere [4]. Careful inspection of the abdominal cavity was performed with a 3CCD camera (Olympus OTV SX2, KeyMed Ltd, Southend on Sea, UK) and 10 mm diameter 30° telescope. Usually a second 10 mm or 5 mm diameter port was inserted, to inspect the initial entry site for proximity to adherent bowel, to retract viscera and elevate the left side of the liver, to perform biopsy of suspicious peritoneal or liver nodules and to facilitate LapUS.

The technique of LapUS has also been described in detail [4]. A 10 mm diameter 7.5 MHz linear array laparoscopic transducer with a 4 cm 'footprint' was used and real-time scanning was observed on the adjacent scanner (Aloka SSD 900, KeyMed Ltd). A systematic sonographic examination of the entire liver was performed, with particular attention to the porta hepatis and para-coeliac regions for suspicious nodes. Laparoscopic examination was considered limited if adhesions precluded a good view of the liver and site of previous colorectal resection. The procedure was considered as having failed if no relevant areas could be inspected satisfactorily. Extensive adhesiolysis was generally avoided in staging laparoscopy. Open surgical exploration was deferred in those patients in whom factors precluding curative resection were identified on laparoscopic assessment.

An attempt at open liver resection without prior laparoscopic staging ('laparotomy group') was made in 338 of 415 (81%) patients who had been deemed potentially resectable following radiological imaging. Liver resections were regarded as potentially curative when the surgeon undertook removal of all macroscopic disease. Histological demonstration of tumour capsular breach during parenchymal transection was regarded as curative on an intention to treat basis. Radical en-bloc resection of locally invaded diaphragm, omentum, small bowel and stomach were included in this category of potentially curative surgery. However, patients with diffuse peritoneal or omental carcinomatosis, or extrahepatic tumour involving coeliac nodes, were typically regarded as

inoperable and their operations were concluded following appropriate biopsies.

Laparotomy was usually performed via an upper midline incision with right subcostal extension. Following careful adhesiolysis and mobilization of the liver, inspection, palpation and intraoperative ultrasound examination of the liver and extrahepatic tissues were performed and a final decision was made regarding resectability. Details regarding the technique of liver resection, typically using the techniques of low central venous pressure anaesthesia and 'bloodless' dissection using the cavitron ultrasonic surgical aspirator (CUSA Ex, Valleylab Inc., Amersham, Bucks, UK) and argon beam coagulation, have been described previously [13].

The principal study outcome measure was the decision to proceed with liver resection with curative intent, or its abandonment, following laparoscopic staging (laparoscopy group, $n=77$) or surgical exploration (laparotomy group, $n=338$). The outcomes were analysed and compared. Patients undergoing laparoscopic liver resection or redo liver resection for colorectal metastases were not included in the study. Neither radiofrequency ablation nor hepatic artery infusion techniques were employed in patients found to be unresectable at laparoscopy or laparotomy in this study.

Results

In all, 77 of 415 patients comprised the laparoscopy group (19%), in whom some 112 previous laparotomies had been performed. Twelve patients had stomas (16%). Satisfactory access to the peritoneal cavity was achieved in 76 of 77 patients (99%) and, in 3 patients (4%), access to the peritoneal cavity required attempts at cut-down at more than one site. Only limited laparoscopic examinations were achieved due to adhesions in 10 patients (13%).

Serious adverse events were recorded in three patients (4%), two of which involved the laceration of small bowel loops adherent to the anterior abdominal wall. In each instance the small bowel injury was identified immediately and repaired by primary suture. Postoperative recovery was uncomplicated and both patients were discharged home within 2 days. Both patients did undergo liver resection. One patient, in whom no tumour dissemination had been discovered at laparoscopy, presented with a late laparoscopic port site metastasis 5 months after abandonment of attempted liver resection because of intrahepatic tumour encroachment upon the hepatic venous confluence.

The impact of laparoscopic staging on clinical management decisions, and the outcomes in patients in whom liver resection was attempted, are shown in Figure 1. Sixteen of 77 (21%) patients in the laparoscopy group were found to have factors precluding liver resection with curative intent because of

peritoneal carcinomatosis ($n=7$), multiple/bilobar metastases ($n=5$), malignant regional lymphadenopathy ($n=4$) and/or insufficient residual liver volume ($n=3$). LapUS alone was responsible for upstaging four patients (5%) in whom laparoscopic inspection had demonstrated no adverse findings (malignant regional lymphadenopathy and/or bilobar metastases).

Forty-one of 415 patients (10%) had previously been subjected to biopsy of their potentially resectable liver lesions, 9 (22%) of whom underwent laparoscopic staging. Of these nine patients, one had histologically proven malignant body wall seeding which was excised at the time of liver resection following negative laparoscopic biopsy of a suspicious peritoneal nodule. The other 32 biopsied patients proceeded directly to laparotomy, 5 of whom were not resected because of peritoneal carcinomatosis, while the other 27 patients underwent curative liver resection.

Four patients in whom no absolute contraindications to liver resection were discovered at laparoscopy subsequently failed to proceed to operation. One of these patients declined the offer of definitive surgery. Evidence for extrahepatic tumour was defined following concurrent imaging in three of these patients.

Fifty-seven patients in the laparoscopy group proceeded to surgical exploration, in 50 (88%) of whom hepatic resection on an intention to treat basis was achieved successfully. Findings contraindicating liver resection were encountered in the remaining seven patients (12%) who had been staged laparoscopically and whose operations were subsequently abandoned. Reasons for laparoscopic failure included occult extrahepatic disease comprising regional lymphadenopathy ($n=4$), and the discovery of more extensive intrahepatic tumour where it was not thought possible to achieve a radical margin of resection because of tumour invasion of the hepatic venous confluence and/or inferior vena cava ($n=3$). However, as previously described, one patient in whom laparoscopy had been limited by adhesions, and in whom a heavy burden of post-chemotherapy necrotic lymph nodes was the reason for abandoning subsequent attempts at liver resection, underwent curative hepatic resection 5 months later following a favourable 'test of time'. More extensive intrahepatic disease than had been identified laparoscopically was encountered at operation in another patient and an extended right hepatectomy plus local resection of an unexpected segment 3 metastasis was performed. Although a non-radical resection margin was obtained, this patient was not regarded as having had a false negative laparoscopy because of the clinical decision to proceed with liver resection with curative intent on an intention to treat basis.

In the laparotomy group, 311 of 338 patients (92%) achieved liver resection, while operation was abandoned in 27 patients (8%) due to the discovery of

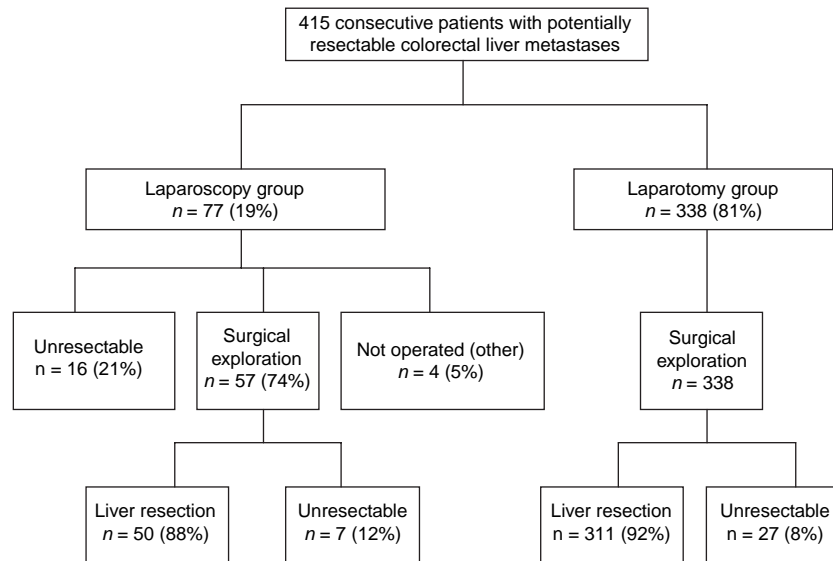


Figure 1. Outcome in 415 consecutive patients with colorectal liver metastases considered potentially suitable for liver resection.

unexpected intrahepatic disease ($n = 14$), extrahepatic disease ($n = 14$) or both intrahepatic and extrahepatic disease ($n = 1$).

Discussion

Laparoscopic staging performed in the aftermath of major bowel resection, stoma formation and/or systemic chemotherapy can be technically challenging and is associated with a small but definite risk of serious complications. Our experience confirms that safe laparoscopic access is almost always feasible. In this regard our results compare favourably with those of others [10,14], and highlight the necessity of early recognition and repair of the occasional visceral injury. The single instance of late laparoscopic port site seeding in this series draws attention to a serious but extremely rare complication in patients with colorectal liver metastases. Despite this, support for a continuing role for staging laparoscopy in selected patients with colorectal liver metastases under consideration of curative liver resection has been provided.

Although the impact of laparoscopic staging in detecting 'occult' disease has been evaluated extensively in the context of patients with a variety of hepatobiliary, pancreatic and oesophagogastric malignancies [7,15,16], there has been a relative paucity of evidence regarding the precise contribution of laparoscopy to the evaluation of patients with potentially resectable colorectal liver metastases.

Cross-sectional imaging based on CT and/or MRI techniques has evolved significantly over the last decade [17] and remains at the core of the staging algorithm for such patients. However, these modalities can be fallible in detecting low volume intrahepatic and extrahepatic disease in a proportion of patients. While countless published series have testified to the effectiveness of liver resection in patients

with colorectal liver metastases, details quantifying the number of patients understaged in this way and subjected to unnecessary (non-curative) laparotomy have tended to be elusive. In this regard, the experience of Jarnagin and colleagues at Memorial Sloan Kettering Cancer Center between 1992 and 1997 provided a reality check [3]. Of 416 consecutive patients with colorectal liver metastases deemed potentially operable, 79% were resected as planned, while factors precluding resection (extrahepatic in 49%, intrahepatic in 51%) were encountered in 87 patients (21%).

The negative effects of such unnecessary operations are self-evident, and include physical (postoperative pain, immunosuppression, potential complications), psychological (anxiety, false hope) and health economic factors. Palliative surgical interventions such as ablation techniques and regional hepatic artery implantation therapy have not been proven to be beneficial in this scenario and may not justify laparotomy, while subsequent delays in commencing palliative chemotherapy are inevitable [11].

In this study, 16 of 77 patients (21%) were spared this fate as a direct consequence of laparoscopic staging. This seems a reasonable yield in support of both the technique and the selection policy practised in this patient group. Comparison with previous studies is complex as the results of others have varied widely. Previous work performed during the 1990s tended to report higher yields of 27–36% following laparoscopic staging as a prelude to liver resection [4–7]. However, these series comprised patients with a variety of liver tumours, not just those with colorectal liver metastases, and followed radiological studies which might be considered inferior by contemporary standards. In patients specifically with potentially resectable colorectal liver metastases, modest laparoscopic yields of only 5–14% have

been reported in some more recent studies [8,10,11], which are at variance with the higher incidences of management-changing findings of 33% [9] and 67% [14] described in other contemporary reports. Indeed, Thaler and colleagues achieved liver resection in just 23 of 69 potentially operable patients (33%) as a direct consequence of the findings of staging laparoscopy with ultrasound despite having been preceded by routine spiral contrast CT scans and the liberal use of PET-CT [14]. Intangibles which may have influenced such disparity in outcomes include varying quality of pre-laparoscopy investigations, the degree of selectivity exercised in performing laparoscopic staging and differences in the indications for and practice of curative liver resection performed within individual institutions.

The adoption of selective laparoscopic staging in 'at risk' patients with colorectal liver metastases has accompanied substantial improvements in modern radiological imaging techniques and concerns regarding diminishing diagnostic yields when laparoscopy is performed routinely [8,10]. In recent years, the concept of the clinical risk score (CRS) as a basis for selective laparoscopic staging has been developed and popularized by Jarnagin and co-workers [8]. The CRS is calculated from up to five criteria, namely lymph node positive primary tumour, disease-free interval (<12 months), number of hepatic tumours (>1), serum carcinoembryonic antigen level (>200 ng/ml), and size of largest hepatic tumour (>5 cm diameter). The overall yield of laparoscopic staging in 103 patients was 14%, rising from 4% in those with a CRS = 2 up to 27% in patients with a CRS > 2 [8]. Further work from the same group has validated these findings, citing the avoidance of unnecessary laparotomy following laparoscopic staging in 24% of that subgroup of patients with a CRS of 4 or 5 [11]. Similarly, Metcalfe and colleagues [9] selected 24 of 73 patients with potentially operable colorectal liver metastases for staging laparoscopy on the basis of shorter disease-free intervals and multiplicity of lesions, 8 of whom were found to be unresectable at laparoscopy (33%).

While the specific criteria for selection adopted in the present study differ from those underpinning the CRS, the results generally concur with those of recent studies seeking to assess the impact of selective staging laparoscopy [8,9,11] and by and large based on a similar concept. Furthermore, the relatively low incidence of non-therapeutic laparotomy (8%) in the laparotomy group in the present study reproduces the findings of Metcalfe et al. (6% unresectable) [9], and appears to endorse selective laparoscopic staging based on these criteria.

The inclusion for laparoscopic staging of those patients with potentially operable colorectal liver metastases in whom injudicious attempts at biopsy had been carried out was of particular interest. Such patients may justifiably be considered at increased risk

of extrahepatic tumour dissemination and poorer oncological outcome [18,19]. However, laparoscopy had minimal impact in detecting post biopsy seeding in those patients examined and does not seem to be indicated for this reason alone.

The fallibility of laparoscopic staging itself is reflected by the 7 patients out of 57 (12%) in whom false negative laparoscopies resulted in unnecessary laparotomy plus the one non-radical resection. This affirms the experience of others where similar outcomes followed 9% [10] and 17% [9] of laparoscopic examinations. While views of peritoneal and omental seeding may be obscured by adhesions in some cases, it is usually undetected malignant regional lymphadenopathy which accounts for failure during laparoscopy to detect extrahepatic disease [4,8,11,14]. The use of LapUS-guided fine-needle aspiration (FNA) or assessment of lymph nodes might be expected to improve the detection rate, but this was not our experience. Intrahepatic disease contraindicating attempts at resection, particularly deep-seated tumour involving the hepatocaval area, may not always be apparent at laparoscopy (despite using LapUS) and accounted for half of our laparoscopic 'misses'.

In much the same way that intraoperative ultrasonography has become an indispensable and ubiquitous technique among hepatobiliary surgeons [20], so it has been suggested that LapUS may address the lack of tactile feedback and enhance the yield of laparoscopy in detecting such occult disease [4,6,7,16]. However, details regarding the precise contribution of LapUS over and above that of laparoscopy in patients with colorectal liver metastases have been vague. Our attempt to quantify its role defined four patients (5%) who were upstaged by the findings of LapUS alone, representing a small but important contribution.

Malignant regional lymphadenopathy is a recognized pitfall in the staging of patients with colorectal liver metastases [8] and, despite the use of LapUS, continued to confound efforts at preoperative detection in this series. Malignant hilar and para-coeliac nodes may not necessarily be enlarged or exhibit specific sonographic features, and their subtle morphology can present a diagnostic challenge even during laparotomy and trial dissection. Nevertheless, in recent work reported by Thaler and colleagues, nodal disease was successfully detected in 11 of 12 documented cases using staging laparoscopy with LapUS, in patients in whom both CT and PET-CT had been performed routinely [14]. They excised and sent for immediate pathological sectioning all lymph nodes that were round, heterogeneous or displacing adjacent tissues.

The novel biological imaging technique of PET-CT does, however, continue to attract interest as a non-invasive means of improved staging in patients with potentially operable colorectal liver metastases. While initial enthusiasm for PET-CT may have been

tempered by its limitations in evaluating intrahepatic disease and its poor specificity, recent reports comparing PET-CT with good quality contrast-enhanced CT in patients with metastatic colorectal cancer have demonstrated its superior sensitivity in detecting occult extrahepatic disease [21,22], locoregional recurrence of primary colorectal malignancy and intrahepatic recurrence of metastases following liver resection [22]. Further study is required to determine whether laparoscopic staging becomes complementary to or supplanted by PET-CT in this role.

Overall, approximately one-fifth of all patients presenting with potentially resectable colorectal liver metastases were selected for laparoscopic staging having had 'state of the art' cross-sectional imaging. About a fifth of these patients were found to have occult disease which averted unnecessary surgical exploration. These findings support the role of laparoscopy and LapUS in complementing the conventional staging algorithm and as a problem-solving modality in borderline cases of indeterminate resectability.

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