Laparoscopy and Laparoscopic Ultrasound

N.J. Peel and O.J. Garden

11.1 Introduction

Hilar cholangiocarcinoma usually presents late with a poor prognosis that results in diagnostic and therapeutic challenges for the clinician. For individuals diagnosed with cholangiocarcinoma, surgery currently offers the only potential curative option, however a laparotomy and surgical resection of localized disease is itself associated with significant morbidity and mortality [1–3]. For patients diagnosed with advanced disease, life expectancy is short and survival in those who have incomplete tumour resection is identical to patients who receive palliative therapy alone for non resectable illness [1]. The benefits of avoiding laparotomy can therefore not be overemphasized and include less pain and morbidity, decreased hospital stay, decreased overall cost and earlier initiation of palliative therapy [2, 3]. Consequently, adequate staging is of utmost importance to prevent unnecessary laparotomy in those with advanced illness not suitable for potentially curative surgery. Whenever surgical palliation is preferred, laparotomy is indicated, regardless of tumour resectability. Nevertheless, despite improvements in imaging, the incidence of non therapeutic laparotomies remains high, up to 46 % in some studies [1].

Laparoscopy has been used as a diagnostic staging tool for some years in hepato-pancreato-biliary tumours. Its main function is to further stage those patients deemed suitable for surgical resection after undergoing conventional radiological assessment. Hilar cholangiocarcinomas are often small and tend not to form a bulky mass. For this reason they are difficult to visualise and therefore stage accurately on any

standard imaging modality [4]. CT and MRI imaging are usually accurate in identifying portal vein occlusion, however, more discrete tumour invasion is often missed [4]. Even with the most sophisticated radiological imaging, the false-negative rate for identifying small liver (Fig. 11.1), omental or peritoneal (Fig. 11.2) deposits is approximately 10–30 % [5]. Hilar cholangiocarcinoma in particular tends to be unresectable and the surgeon is often faced with major

Fig. 11.1 Small liver metastasis on under surface of left lobe of liver

N.J. Peel, MBChB, BSc, MRCS(Glas)
Clinical Research Fellow, University of Edinburgh,
Royal Infirmary of Edinburgh, Edinburgh, UK

O.J. Garden, BSc, MBChB, MD, FRCS(Glasg), FRCS(Ed),
FRCP(Ed), FRACS(Hon), FRCSC(Hon) (✉)
Clinical and Surgical Sciences (Surgery),
University of Edinburgh, Royal Infirmary of Edinburgh,
Edinburgh, UK
e-mail: o.j.garden@ed.ac.uk

Fig. 11.2 Peritoneal dissemination of cholangiocarcinoma

discrepancies between staging performed by radiological imaging alone, and actual findings at laparotomy [4]. Therefore, the main benefits of laparoscopy include the increased likelihood of visualizing small metastatic tumour deposits on the surface of the liver and peritoneum which would otherwise go undetected by conventional radiological techniques alone.

There are limited studies on the added benefits of incorporating this modality into the staging of hilar cholangiocarcinoma and the outcomes appear to be influenced by a multitude of factors including the quality of the conventional radiological imaging, the timing of the laparoscopy in the staging process and the expertise of the surgeon performing the procedure [4–7]. Adding laparoscopic ultrasound (LUS) may further aid staging and increase the yield of laparoscopy by highlighting radiologically undetectable intrahepatic metastases and localized vascular invasion [4, 7]. Again the chief limitation of LUS is that it is highly operator dependent and, even in the hands of the most experienced of operator, biopsies are difficult to obtain [8].

The low yield of laparoscopy in identifying patients unsuitable for laparotomy is the primary reason that it has not been accepted as universal practice in all centres [3–7, 9, 10]. It is also likely that as non-invasive radiological imaging techniques improve, the yield of staging laparoscopy will decrease. Furthermore, it has been postulated that laparoscopy could be useful in guiding palliative treatment by identifying patients with locally advanced disease suitable for chemoradiation from those with metastatic disease suitable for chemotherapy alone [4].

11.2 Indications

Staging laparoscopy is recommended for patients who have been diagnosed with cholangiocarcinoma that has been demonstrated to be potentially curable by surgical excision after a full battery of radiological investigations. A second indication to perform a laparoscopy would be to confirm the presence of locally advanced disease as opposed to metastatic, in order to guide neo-adjuvant palliative treatment although evidence for this is less robust [11]. Contra-indications to laparoscopy are signs of duodenal obstruction as the patient will require definitive surgery to relieve the obstruction.

11.3 Technique

In our institution, staging laparoscopy and laparoscopic ultrasound are generally performed separately to subsequent laparotomy. This is mainly due to logistical reasons relating to anaesthetic planning and patient preference but in some centres both procedures are performed at a single sitting. Although this may present challenges with effective theatre time management, carrying out staging laparoscopy and laparotomy in a single session may be more beneficial to the individual patient as it would prevent two procedures and two hospital visits.

Staging laparoscopy is performed under general anaesthetic with the patient placed supine and the principle operating surgeon positioned on the left side of the patient. Pneumoperitoneum is established in the standard fashion, gaining access using an open "Hassan" technique and insufflating with CO_2 at a pressure of 12–15 mmHg through a 12 mm infra-umbilical port [12]. A second 12 mm port is placed in the right mid quadrant.

A 30° scope is inserted through the infra-umbilical port and the abdominal cavity is visualized. A careful inspection of the peritoneum is undertaken to identify any tumour deposits. Intraabdominal organs are inspected in turn, the visceral peritoneum, the liver including the undersurface, the anterior aspect of the stomach, the lesser and greater omentum, the diaphragm and porta are inspected. By retracting the greater omentum superiorly, the small bowel and root of the mesentery can be identified [12]. Suspicious lesions should be biopsied at the end of the procedure using a biopsy forcep or a biopsy needle [4]. The biopsies should be taken under direct laparoscopic vision or by laparoscopic ultrasound guidance [4, 12].

Laparoscopic ultrasound is best performed using a high-resolution flexible tip linear array transducer [12]. Isotonic saline can be introduced to the peritoneal cavity if required to provide an acoustic window, and decreasing the abdominal pressure to 7–8 mmHg has been shown to improve contact with the liver surface [4, 12]. The ultrasound probe should be inserted through both ports to allow imaging in two planes. The probe is normally sterilized or can be wrapped in a sterile cover sheet, filled with sterile ultrasonic gel. A systematic approach should be taken to examine the liver starting with the identification of standard landmarks. The liver parenchyma should be investigated for signs of intrahepatic metastatic lesions, which can appear as hyper-, iso-, or hypo-echoic

[12]. Furthermore, the portal triad should be examined and its relationship to the primary tumour should be considered [12]. The portal structures are viewed by inserting the probe through the sub umbilical port and placing it on the hepatoduodenal ligament [12]. This allows the surgeon to view the inferior vena cava posteriorly [12]. If the probe is then rotated clockwise, the portal vein, bile duct, and hepatic artery may be inspected [12].

Withdrawing the probe allows the portal vein to be followed to the spleno-portal confluence and continues down the SMV [12]. A loss of tissue planes between the primary tumour and the surrounding vessels suggests vascular invasion [12]. This part of the procedure is particularly operator dependent as placing too much pressure on the probe can create images consistent with that of vascular involvement. A further indication of vascular involvement that can be demonstrated by laparoscopic ultrasound is a fixed stenosis of the vessel in more than one plane [4]. For hilar cholangiocarcinoma in particular it is important to assess the primary lesion in order to determine its proximal and distal extent, radial extension and lymph node metastases [12]. Involved lymph nodes appear as hyper-echoic, less well circumscribed nodes. Suspicious nodes should be confirmed by biopsy [12]. After biopsies have been taken, the wounds are inspected for excess bleeding, the ports are removed and the wounds are closed in the usual fashion.

11.4 Safety and Complications of Staging Laparoscopy

Staging laparoscopy is an established safe procedure. It has a low morbidity with complications reported in 0.15–3 % of cases, and the mortality is negligible (0.05 %) [4, 13].

The introduction of the infra umbilical trocar is the most hazardous part of any laparoscopic procedure. This is due to the risk of injury to the abdominal aorta or other vulnerable parts of the vascular tree and the risk of injury to the bowel. Penetrating vascular injuries can be catastrophic and mortality in these patients have been reported to be up to 17 % however the incidence of such events remains low (0.001–0.005 %) [14]. Similarly, the mortality associated with a bowel injury during staging laparoscopy has been reported in some studies to be 3.6 % although the incidence is low at 0.13 % [15]. Obviously, if a patient has undergone previous abdominal surgery then the incidence of complications rises. In our unit, a Hasson open technique is used to gain access to the peritoneum. Using this technique does not remove the risk of delayed injury to the bowel from injury by diathermy, however, we believe that it does reduce the risk of penetrating injury to the bowel and vasculature and increases the chance of any injury being directly visualized and therefore identified early.

van Dijkum and colleagues studied prospectively a series of 420 patients undergoing staging laparoscopy for upper gastrointestinal cancers [16]. Following the procedure, 1 % of patients had major complications which included anaphylactic shock, small bowel injury and bile leakage following a liver biopsy [16]. A further 3 % of patients suffered minor complications such as wound infections, wound haematomas, post operative pain, aspiration pneumonia, post operative urinary retention and incisional hernia [16]. All patients survived the procedure and the mean discharge time was 1.5 days [16]. Shoup and his colleagues in New York corroborated these findings in a similar study with a comparable group of patients [17].

Port site metastases are often sited as a major complication of staging laparoscopy and are much feared as the consequences for the patient may be devastating. The expected risk, however, is probably overestimated and is not supported by present evidence [4]. In the study of van Dijkum, port site metastasis occurred in 2 % of patients all of whom had metastatic disease at the time of staging laparoscopy and had evidence of very advanced disease when the port site lesions were identified [16]. Shoup et al. reported an even lower incidence (0.8 %). However, although small, the risk of port site metastasis should still be respected and it is recommended that attempts at biopsy of hilar cholangiocarcinoma should be restricted to suspected metastases at staging laparoscopy to pathologically confirm a diagnosis [4]. The risk of unnecessary laparotomy significantly outweighs that of port site metastasis which does not influence the outcome for the patient if metastatic disease is already present [4].

11.5 Peritoneal Washings

Cytological analysis of peritoneal washings, obtained during staging laparoscopy has been established as a means of increasing laparoscopic yield in many solid organ malignancies [18–22]. Peritoneal lavage has been shown to identify occult disease in both gastric and pancreatic cancers that were otherwise deemed resectable [18]. Burke and colleagues demonstrated that patients with seemingly resectable gastric cancer but positive peritoneal cytology had a similar prognosis to patients diagnosed with metastatic disease [18]. Similarly, for pancreatic cancer, patients found to have malignant cells in peritoneal lavage fluid despite having no overt signs of metastatic deposits have a similar prognosis to those diagnosed with disseminated disease [20, 21].

On the basis of this knowledge, Martin and colleagues examined peritoneal washings of 26 patients with confirmed hilar cholangiocarcinoma that were deemed suitable for resection by radiological staging [22]. Malignant cells were identified in only two of the patients who were also found to have gross peritoneal deposits at laparoscopy. Interestingly nine other patients were found to have metastatic disease present at laparoscopy but had negative washings. It would therefore seem that unlike pancreatic and gastric cancers, peritoneal lavage does not provide any useful additional

information in the staging of hilar cholangiocarcinoma and should not be routinely practiced.

11.6 Literature Review

There have been a small number of studies in recent years that have examined the benefits of staging laparoscopy and laparoscopic ultrasound in patients with hilar cholangiocarcinoma. At the Memorial Sloan-Kettering Cancer Centre, Weber et al. conducted a large study to investigate the use of staging laparoscopy in patients with both gallbladder cancer and hilar cholangiocarcinoma [2]. Fifty-six patients who were diagnosed with potentially resectable hilar cholangiocarcinoma were included, 14 (25 %) of whom were identified as having metastatic disease at staging laparoscopy. Forty-two patients therefore proceeded to open laparotomy, but 19 were shown to have unresectable cancer at surgery. In this study, laparoscopy detected the majority (83 %) of patients with peritoneal or liver metastasis but failed to identify those with locally advanced tumours and most with nodal metastasis [23]. The yield of laparoscopy (i.e. the number of patients who were identified as unsuitable for resection) in the New York experience was 25 %, therefore the majority of patients did not benefit from the procedure. Weber and his colleagues attempted to identify patients most at risk of occult metastatic disease to target the use of staging laparoscopy more effectively. They analysed the yield of laparoscopy with respect to the MSKCC T staging system (Table 11.1) that assesses local tumour-related factors present on preoperative imaging [24]. This staging system has previously been shown to predict survival, resectability, and the likelihood of metastatic disease [24]. They found that as T stage advanced so too did laparoscopic yield. The yield increased from 9 % in patients with T1 tumours to 36 % in those with T2/T3 tumours. The authors concluded that staging laparoscopy should be targeted at those diagnosed with T2/T3 tumours as this group had the greatest yield. It is unclear however if T staging was based on preoperative imaging alone or was modified after intra operative findings. Laparoscopic ultrasound was carried out in 23 patients as part of their staging assessment. No additional patients with unresectable disease were identified solely using this investigation, it is uncertain therefore if the laparoscopic yield would have been increased had all 56 patients been investigated with laparoscopic ultrasound.

Our own group studied patients with suspected hilar cholangiocarcinoma over 11 years (1992–2003) [8, 23]. Eighty-four patients deemed potentially suitable for resection after standard radiological investigations underwent staging by laparoscopy and laparoscopic ultrasound. Twenty of the 84 patients (24 % yield) were felt to be unresectable after

Table 11.1 MSKCC revised preoperative staging system for patients with hilar cholangiocarcinoma

T Stage	Description
1	Tumour involving biliary confluence ± unilateral extension to 2° biliary radicles
	No liver atrophy or portal vein involvement
2	Tumour involving biliary confluence ± unilateral extension to 2° biliary radicles with ipsilateral portal vein involvement ± ipsilateral hepatic lobar atrophy
	No main portal vein involvement
3	Tumour involving biliary confluence + bilateral extension to 2° biliary radicles
	OR unilateral extension to 2° biliary radicles with contralateral portal vein involvement
	OR unilateral extension to 2° biliary radicles with contralateral hepatic lobar atrophy
	OR main or bilateral portal venous involvement

Adapted from Weber et al. [23]

staging laparoscopy alone as 15 patients were found to have metastatic peritoneal or liver deposits and 5 had histologically confirmed nodal disease outside the resection field. The yield was increased to 42 % after laparoscopic ultrasound was added and identified a further 14 patients, 1 of whom had an intra hepatic metastasis and 13 who were found to have locally advanced disease. Despite the addition of laparoscopic ultrasound and its apparent ability to detect locally advanced disease, 10 of the 19 patients undergoing resection were found to have positive resection margins, indicating that in practice, identifying patients with local invasion continues to represent a significant challenge.

The patients in the Edinburgh study were again graded according to the MSKCC T staging system. As in Weber and colleagues' study, it was also noted that laparoscopic yield increased with T stage. The yield for T1, T2, and T3 tumours was 26, 37 and 69 % respectively. Fourteen, 25 and 5 patients in the T1, T2 and T3 groups respectively were found to have resectable disease after staging however, at laparotomy, only eight, 11 and one patient in each T stage group did indeed have cancer that was potentially curable be surgery. Interestingly, the reasons for this differed between T stage groups. In the T1/T2 groups, metastatic disease was most likely to be the culprit, however in the T3 group local invasion was the primary reason for unresectability. This suggests that a different biological process is taking place in the T3 group.

The yield from staging laparoscopy and laparoscopic ultrasound in this study was 42 % with an overall accuracy of 53 %. These figures are higher than that of Weber et al. The Edinburgh study was conducted over a longer time period during which the quality of radiological imaging has undoubtedly varied and the selective approach to employing

Table 11.2 Studies on the value of staging laparoscopy and laparoscopic ultrasound for hilar cholangiocarcinoma and detection of unresectable disease at laparotomy

Author	Year	Patients	Study type	Unresectable found at laparoscopy (%)	Unresectable found at laparoscopic ultrasound (%)	Additional unresectable found at laparotomy (%)	Total unresectable patients (%)
Weber et al. [23]	2001	56	Prosp	25	0	34	60
Connor et al. [10]	2005	84	Prosp	24	16	12	52
Tillerman et al. [25]	2002	110	Prosp	41	1	27	67

laparoscopic ultrasound as a staging modality by the MSKCC team may have decreased their overall yield.

In a larger study carried out by Tilleman and colleagues in the Netherlands [25], 110 patients with cholangiocarcinoma were investigated between 1993 and 2000, for tumour that was deemed potentially resectable by standard radiological imaging [25]. In these patients who were staged using laparoscopy without laparoscopic ultrasound, the results were similar to that of the Edinburgh group. Laparoscopy revealed histologically proven incurable disease in 41 % of patients with an accuracy of 56 %. Again, the authors comment that radiological staging has substantially improved in recent years both with the introduction of spiral CT with 3 mm slides and with the improvements in endoscopic ultrasonography [25], thereby accounting for the high yield in this study. The findings of all three studies are summarised in Table 11.2.

Conclusion

Patients with hilar cholangiocarcinoma often have unresectable disease that is not evident on pre-operative radiological imaging. Laparoscopic staging can prevent unnecessary laparotomies in around 30 % of patients. It would appear that the addition of laparoscopic ultrasound, is useful, and significantly improves the yield. Although the yield of laparoscopic staging is reasonable, the accuracy remains poor and unfortunately the majority of patients who undergo laparoscopic staging do not benefit from it. Unresectable disease in patients that is not detected at laparoscopy is most often due to locally advanced disease. Detecting this remains the biggest challenge in improving the yield and accuracy of laparoscopic staging. It is likely, as radiological technology improves, that the yield of laparoscopic staging may decrease as the majority of patients with non resectable disease will be identified pre-operatively, but until then many centres will continue to include this modality in its investigative and staging algorithm.

References

1. Goere D, Wagholikar GD, Pessaux P, et al. Utility of staging laparoscopy in subsets of biliary cancers. Surg Endosc. 2006;20:721–5.
2. D'Angelica M, Fong Y, Weber S, et al. The role of staging laparoscopy in hepatobiliary malignancy: prospective analysis of 401 cases. Ann Surg Oncol. 2002;10(2):183–9.
3. Rumstadt B, Schwab M, Schuster K, et al. The role of laparoscopy in the pre-operative staging of pancreatic carcinoma. J Gastrointest Surg. 1997;1:245–50.
4. van der Gaag NA, Busch ORC, Bemelman WA, et al. Laparoscopy in staging and assessment of hepatobiliary disease. In: Garden OJ, editor. Hepatobiliary and pancreatic surgery. 4th ed. Saunders: Elsevier; 2009. p. 37–53.
5. Carlos U, Covera MD, Sharon M, et al. Role of laparoscopy in the evaluation of biliary tract cancer. Surg Oncol Clin N Am. 2002; 11:877–91.
6. Brooks AD, Mallis MJ, Brennan MF, et al. The value of laparoscopy in the management of ampullary, duodenal and distal bile duct tumours. J Gastrointest Surg. 2002;62:139–45.
7. Jarnagin WR, Conlon KC, Bodniewicz J. A clinical scoring system predicts yield of diagnostic laparoscopy in patients with potentially resectable hepatic colorectal metastasis. Cancer. 2001;91:1121–8.
8. White R, Pappas TN. Laparoscopic staging for hepatobiliary carcinoma. J Gastrointest Surg. 2004;8:920–2.
9. D'Angelica M, Fong Y, Weber S. The role of staging laparoscopy in hepatobiliary malignancy: prospective analysis of 401 cases. Ann Surg Oncol. 2003;10:183–9.
10. Connor S, Barron E, Wigmore SJ, et al. The utility of laparoscopic assessment in the preoperative staging of suspected hilar cholangiocarcinoma. J Gastrointest Surg. 2005;9:476–80.
11. Gouma DJ, van Nieveen DEJM, de Wit LT, et al. Laparoscopic staging of biliopancreatic malignancy. Ann Oncol. 1999;10: s33–6.
12. Joseph S, Connor S, Garden OJ. Staging laparoscopy for cholangiocarcinoma. HPB. 2008;10:116–9.
13. Boyd WP, Nord HJ. Diagnostic laparoscopy. Endoscopy. 2000; 32:153–8.
14. Bateman BG, Kolp LA, Hoeger K. Complications of laparoscopy-operative and diagnostic. Fertil Steril. 1996;66:30–5.
15. van der Voort M, Heijnsdijk EA, Gouma DJ. Bowel injury as a complication of laparoscopy. Br J Surg. 2004;91:1253–8.
16. Niveen van Dijkum EJ, de Wit LT, van Delden OM, et al. Staging laparoscopy and laparoscopic ultrasound in more than 400 patients with upper gastrointestinal carcinoma. J Am Coll Surg. 1999;189: 459–65.
17. Shoup M, Brennan MF, Karpeh MS, et al. Port site metastasis after diagnostic laparoscopy for upper gastrointestinal tract malignancies: an uncommon entity. Ann Surg Oncol. 2002;9:632–6.
18. Burke EC, Karpeh MS, Conlon KC, et al. Peritoneal lavage cytology in gastric cancer: an independent predictor of outcome. Ann Surg Oncol. 1998;5:411–5.
19. Makary MA, Warshaw AL, Centeno BA, et al. Implications of peritoneal cytology for pancreatic cancer management. Arch Surg. 1998;133:361–5.
20. Leach SD, Rose JA, Lowy AM, et al. Significance of peritoneal cytology in patients with potentially resectable adenocarcinoma of the pancreatic head. Surgery. 1995;118:472–8.

21. Jimenez RE, Warshaw AL, Rattner DW, et al. Impact of laparoscopic staging in the treatment of pancreatic cancer. Arch Surg. 2000;135:409–14.

22. Martin II RCG, Fong Y, DeMatteo RP, et al. Peritoneal washings are not predictive of occult peritoneal disease in patients with hilar cholangiocarcinoma. J Am Coll Surg. 2001;193:620–5.

23. Weber SM, DeMatteo MD, Fong Y, et al. Staging laparoscopy in patients with extrahepatic biliary carcinoma. Ann Surg. 2001; 235:392–9.

24. Jarnagin WR, Fong Y, DeMatteo RP. Staging analysis of resectability and outcome in 225 patients with hilar cholangiocarcinoma. Ann Surg. 2001;234:540–8.

25. Tilleman EHBM, de Castro SMM, Busch ORC, et al. Diagnostic laparoscopy and laparoscopic ultrasound for staging of patients with malignant proximal bile duct obstruction. J Gastrointest Surg. 2002;6:426–30.