ORIGINAL ARTICLE

Laparoscopic versus open hepatectomy for liver tumours: a case control study

KF Lee 李傑輝
YS Cheung 張宇新
CN Chong 莊清寧
Yvonne YY Tsang 曾頤欣
Wilson WC Ng 吳咏志
Eva Ling 凌曉華
John Wong 黃 創
Paul BS Lai 賴寶山

Objective To evaluate the benefits of laparoscopic versus open resection of liver tumours.

Design Case control study.

Setting Tertiary teaching hospital, Hong Kong.

Patients Data from 25 patients who underwent laparoscopic resections for liver tumours from 2003 to 2006 were compared to a retrospective series of 25 patients who underwent open hepatectomy in a pair-matched design.

Main outcome measures Duration of operation, operative morbidity and mortality, blood loss, tumour resection margin, analgesics usage, days to return to an oral diet, duration of postoperative hospital stay, and survival of patients with malignancy.

Results The demographic data and the tumour characteristics were comparable in the two patient groups, as were mortality (0% in both groups) and morbidity rates (4% in both groups). Two (8%) of the patients having laparoscopic resections were converted to open surgery. There was no statistically significant difference between the two groups in terms of operating time or resection margins. However, the laparoscopically treated patients experienced significantly less blood loss (median, 100 vs 250 mL), had shorter hospital stays (median, 4 vs 7 days), were prescribed less analgesia (median morphine dosage, 0.16 vs 0.83 mg per kg body weight), and resumed oral diet earlier (median, 1 vs 2 days). For patients with malignant tumours, there was no significant difference between the two groups in terms of actuarial and disease-free survival.

Conclusion Compared to open hepatectomy, in selected patients laparoscopic liver resection delivers the benefits of decreased blood loss, shorter hospital stay, lesser requirement for analgesics, and an earlier return to an oral diet, without evidence of compromised oncological clearance.

Key words
Hepatectomy; Laparoscopy; Liver diseases; Liver neoplasms; Treatment outcome

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Division of Hepato-biliary and Pancreatic Surgery, Department of Surgery, Prince of Wales Hospital, The Chinese University of Hong Kong, Shatin, Hong Kong
KF Lee, FRCS (Edin), FHKAM (Surgery)
YS Cheung, MB, ChB, MRCS
CN Chong, MB, ChB, MRCS
YYY Tsang, MB, ChB, MRCS
WWC Ng, FRCS (Edin), FHKAM (Surgery)
E Ling, MPhil
J Wong, FRCS (Edin), FHKAM (Surgery)
PBS Lai, MD, FHKAM (Surgery)

Correspondence to: Prof PBS Lai
E-mail: paullai@surgery.cuhk.edu.hk

Introduction

Liver surgeons have been slow to adopt the laparoscopic technique for liver resections. Understandably, they are concerned about the control of bleeding, difficulty in retraction and exposure, and the risk of air embolism. For malignant tumours, many expressed concerns about compromising oncological clearance and tumour seeding in the peritoneal cavity.[1,2] Despite these difficulties, instruments have improved and surgical techniques have been refined to ensure that laparoscopic liver resection is not only feasible and safe, but also beneficial in terms of blood loss, length of hospital stay, and severity of wound pain.[1,2] More than a thousand laparoscopic liver resections have been performed worldwide since 1992, after Gagner et al[1,3] performed the first non-anatomical resection of a liver tumour. Although most of these involved resections of only one or two liver segments,[4-7] major hepatectomies have also been achieved laparoscopically.[8-10] Laparoscopic liver resections are now accepted as safe and feasible for selected patients, but their benefits are not clearly demonstrated. Against this background, we used a pair-matched design to compare the results of laparoscopic hepatectomy with those of the open approach.

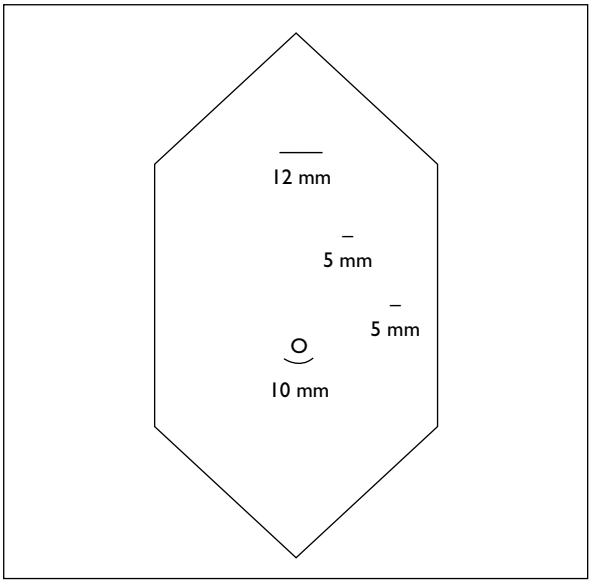


FIG 1. Port sites for laparoscopic left lateral sectionectomy

腹腔鏡相對開腹肝臟腫瘤切除的病例對照研究

目的 與傳統開腹手術比較，探討腹腔鏡肝腫瘤切除術所帶來的可能益處。

設計 病例對照研究。

安排 香港一所三級轉介教學醫院。

患者 2003至2006年期間，以25位用腹腔鏡切除肝臟腫瘤的病人及25位以開腹切除肝臟腫瘤的病人作一對照病例研究。

主要結果測量 手術時間、手術死亡率、術後併發症、出血量、腫瘤切緣、鎮痛藥需求、術後恢復進食時間、術後住院時間，以及惡性腫瘤病人的術後存活率。

結果 兩組病人的人口學數據及腫瘤的特性相近。兩組病人的術後併發症及手術死亡率是一樣的，分別是4%及0%。腹腔鏡切除的一組有兩例（8%）術中轉為開腹切除。兩組之間的手術時間及腫瘤切緣在統計上都沒有差異。但是，腹腔鏡切除的一組相對於開腹的一組在統計上有較少出血量（中位數：100毫升比250毫升），較短住院時間（中位數：4天比7天），較少鎮痛藥需求（中位數每公斤體重：0.16比0.83毫克嗎啡）及較早恢復術後進食（中位數：1天比2天）。在惡性腫瘤病人的組群中，兩種手術方式對術後存活率及無復發存活率並沒有差異。

結論 在選擇性病例中，與傳統開腹手術比較，運用腹腔鏡肝臟切除可以減少出血量、減少住院時間、減少鎮痛藥需求、提早恢復術後進食，而沒有防礙惡性腫瘤的完全摘除。

Methods

Patients

In 2003 we initiated a programme of laparoscopic liver resection, offering this approach to patients with no contra-indications for laparoscopy and a tumour of less than 5 cm in a peripheral segment of the liver, that is in segments 2, 3, 4b, 5, or 6, so long as it was not associated with major vascular or bile duct invasion. Patients were also required to provide informed consent for the procedure. We performed either left lateral sectionectomy (bisegmentectomy 2 and 3) or non-anatomical resections, aiming at a minimum resection margin of 1 cm for all malignant tumours.

From January 2003 to December 2006 we performed 256 liver resections at the Prince of Wales Hospital in Hong Kong. Twenty-five (9.8%) of these were carried out with the laparoscopic technique, and the clinical data were prospectively collected and compared with data from 25 patients who underwent open hepatectomy during the same period. We selected these controls from our computer database and matched them with the laparoscopic resection group for tumour size, tumour site, and type of resection. The same three surgeons performed both techniques. The decision for laparoscopic or open hepatectomy was made before the operation or any diagnostic laparoscopy. Besides, there were no exclusions from either laparoscopic or open resection, based on routine laparoscopic ultrasound. Our statistical analysis included *t* tests for normally distributed data (resection margin) and Mann-Whitney tests for other non-parametric variables. Categorical variables were analysed by Chi squared tests, and actuarial and disease-free survival were compared by log rank tests. Any P value of less than 0.05 was taken to indicate statistical significance.

Operative techniques

When performing the laparoscopic resection we adopted a totally laparoscopic technique without using a handport. For most cases we used three to five laparoscopic ports (5 to 12 mm in diameter), placed according to the tumour location. For left lateral sectionectomy, usually four laparoscopic ports were sufficient (Fig 1). A 10-mm subumbilical port was used for the laparoscope and camera. Working ports included one that extended 12 mm over the epigastrium, and two that extended 5 mm over the subcostal region in the left mid-clavicular and anterior axillary lines, respectively. Laparoscopic ultrasound (Aloka, Tokyo, Japan) was routinely performed to delineate the target lesion and to exclude preoperatively undetected lesions. Vascular inflow or outflow occlusion was not used during

parenchymal transection. In the earlier cases we transected the liver with a cavitron ultrasonic surgical aspirator (CUSA) [ValleyLab, Boulder, US] and a TissueLink device (TissueLink Medical Inc, Dover, US), but in latter cases we used the TissueLink device in conjunction with LigaSure (Valleylab, Boulder, US). Radiofrequency ablation (RFA) [Cool-tip; Tyco Healthcare, Boulder, US] was also used in one case. In all patients, endovascular staplers (Tyco Healthcare, Norwalk, US) were used to divide the larger vascular pedicles, while bleeding from smaller vessels was controlled with metal clips. To avoid the risk of air embolism, we did not use argon beam coagulation for haemostasis. In all cases, we used tissue glue (Tisseel; Baxter, Vienna, Austria) to reinforce haemostasis and prevent bile leakage, but the use of drains at the end of the procedure was left to the discretion of the operating surgeon. All specimens were retrieved in plastic bags through an extended port site, usually at the umbilicus.

We performed open hepatectomies via right subcostal incisions with or without upward midline extensions. In all cases, intra-operative ultrasound was used to facilitate the marking of a transection line and to exclude previously undetected lesions. We only performed the intermittent Pringle manoeuvre in one patient; in most cases we used CUSA and a TissueLink device for liver transection, while diathermy plus CUSA was used in one. In some instances, endovascular staplers were used to transect major vascular pedicles. In all but one patient, tissue glue was used to reinforce haemostasis after completion of the transection. Implementing intra-abdominal drainage was left to the operating surgeon's discretion.

Postoperative care

Regardless of the technique used, all patients were admitted to the intensive care unit immediately after the operation, and discharged to the general ward once their condition was regarded as stable. Postoperative analgesia was mostly given as an opioid on-demand or by patient-controlled doses. No epidural analgesia was used in either group. When patients' pain had diminished, milder analgesics (such as paracetamol or dologesic) were prescribed as required. All patients were encouraged to mobilise early and resume feeding as soon as tolerated. They were discharged home, once the surgeon in-charge considered them fit. Criteria used for discharge included: resumption of adequate oral intake, full mobilisation, and stable liver function tests. Patients with benign diseases were followed up once or twice in the out-patient clinic, and those with malignant diseases at 1 month after the operation, then every 3 months in the first year and then every 6 months thereafter. Tumour markers and liver function tests were checked before each follow-up. Ultrasound or computed tomographic scan was performed every 6 months in the first year and annually thereafter, and whenever tumour marker results or clinical suspicion indicated the possibility of tumour recurrence.

Results

The two patient groups were comparable in terms of age, sex, concurrent medical illness, American Society of Anesthesiologists score, Child's grading, and history of previous abdominal surgery. Two patients in the laparoscopic group and four in the open group had recurrent hepatocellular carcinoma; all six have previously undergone open hepatectomy or RFA. The Table indicates no statistically significant difference between the two groups in this aspect. The percentage of patients with hepatitis B virus infection was 56% in the laparoscopic group and 64% in the open group.

The Table also shows the characteristics of the tumours by patient group. There was no statistically significant difference between number of tumours, tumour sites and size, resection types, and incidence of concomitant cholecystectomy. In the laparoscopic group, two patients had two separate tumours that underwent separate resections, and one patient had three small tumours in the same segment that were excised in a single resection. In the open group, three patients had two separate tumours each, only one of whom had two separate resections.

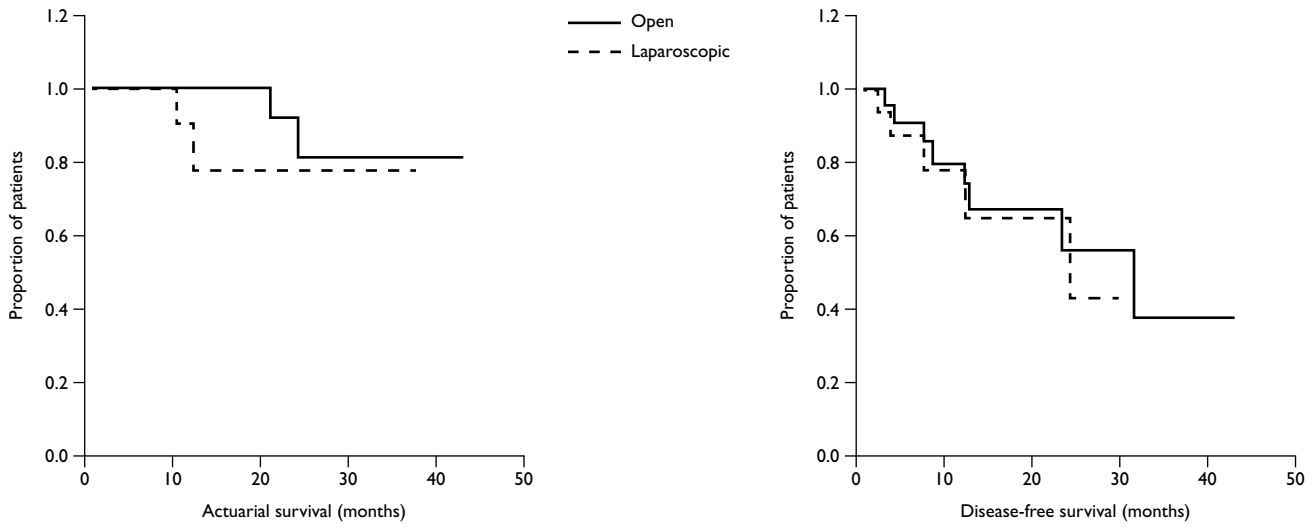
The histological findings from the tumours and non-tumour liver tissues are summarised in the Table. The two groups were very similar in terms of tumour distribution, histological diagnoses, percentages that were malignant, tumour resection margins, and the incidence of background cirrhosis. Moreover, in terms of operative outcome, in the laparoscopic group the operations on two (8%) of the patients were converted to the open technique, for bleeding in one case and lack of progress in the other. Overall, there was no operative mortality in both groups. One of the laparoscopic group patients developed a wound haematoma, and one in the open group developed postoperative ascites. Whilst there was no statistically significant difference between groups in terms of total operating time, in the open group more additional procedures (nine cholecystectomies) were performed than in the laparoscopic group (three cholecystectomies), though this difference too was not statistically significant (Table).

Although one patient in the laparoscopic group received one unit of blood transfusion as opposed to none in the open group, on average estimated blood loss in the laparoscopic group was significantly less (median, 100 vs 250 mL). The laparoscopic group also stayed in hospital for a significantly shorter time

TABLE. Patient and tumour characteristics, and pathological findings and operative outcomes

Characteristic/outcome	Laparoscopic (n=25)	Open (n=25)	P value
Patient characteristics			
Mean age (range) [years]	58 (25-75)	53 (38-70)	0.892
Sex (M:F)	14:11	19:6	0.232
Concurrent ≥2 medical problems	7	8	1.00
Previous abdominal surgery	9	12	0.390
Recurrent HCC* with previous hepatectomy or open radiofrequency ablation	2	4	0.384
American Society of Anesthesiologists			0.991
I	6	5	
II	14	16	
III	5	4	
Child's grading			1.00
A	24	24	
B	1	1	
C	0	0	
Tumour characteristics			
No. of tumours			0.549
1	22	22	
2	2	3	
3	1	0	
Tumour site			0.597
Segment 2-3	18	14	
Segment 4b	7	7	
Segment 5-6	4	6	
Segment 7-8	0	1	
Median tumour size (range) [cm]	2.3 (0.4-9)	2.7 (0.8-13)	0.236
No. of resections			
1	23	24	0.552
2	2	1	
3	0	0	
Type of resection			0.908
Left lateral sectionectomy	11	11	
Non-anatomical resection	16	15	
Concomitant cholecystectomy	3	9	0.098
Finding/outcome			
Histological diagnosis of tumour*			0.165
HCC	16	16	
CRM	3	5	
FNH	4	0	
IHCC	0	1	
Others	2 haemangioma	1 undifferentiated carcinoma, 2 haemangioma	
Malignant tumours	19 (76%)	23 (92%)	0.123
Median resection margin (range) [cm]	1.41 (0-3)	1.36 (0.1-3)	0.803
Co-existing cirrhosis	13 (52%)	8 (32%)	0.152
Median operating time (range) [min]	220 (100-420)	195 (135-285)	0.118
Median blood loss (range) [mL]	100 (20-1500)	250 (50-900)	0.012
Mortality	0 (0%)	0 (0%)	1.00
Morbidity	1 (4%)	1 (4%)	1.00
Median postoperative length of stay (range) [days]	4 (2-8)	7 (3-15)	<0.001
Median time to resume diet (range) [days]	1 (1-3)	2 (1-3)	0.003
Median narcotic dosage (range) [mg morphine per kg body weight]	0.16 (0-1.49)	0.83 (0.05-2.51)	<0.001

* HCC denotes hepatocellular carcinoma, CRM colorectal liver metastasis, FNH focal nodular hyperplasia, and IHCC intra-hepatic cholangiocarcinoma



Patient group	Actuarial survival* (months)	Disease-free survival† (months)	
	Mean (95% CI)	Mean (95% CI)	Median (95% CI)
Laparoscopic (n=19)	32.5 (25.1-40)	21.1 (14.9-27.3)	24.3 (2.5-46.1)
Open (n=23)	39.4 (34.6-44.2)	27.6 (19.9-35.3)	31.6 (16.3-46.9)

* P=0.44, log rank test
† P=0.69, log rank test

FIG 2. Actuarial and disease-free survival for patients with malignancy

(median, 4 vs 7 days), received less narcotic analgesia (median, 0.16 vs 0.83 mg morphine per kg body weight), and resumed an oral diet earlier (median 1 vs 2 days).

Further analysis of the patients with malignant diseases (19 in the laparoscopic and 23 in the open groups) revealed that the patients in the open group were followed up significantly longer (median, range: 21, 4-43.2 months vs 11, 1-38.5 months). In the laparoscopic group, five patients suffered a recurrence, two of whom died. In the open group, eight patients had recurrences, two of whom died. These patients had recurrences in other parts of the liver with or without lung metastasis. We observed no port-site metastasis or peritoneal recurrence. The actuarial and disease-free survival of the two groups were not significantly different (Fig 2). The median disease-free survival was 24 months for the laparoscopic group and 32 months for the open group.

Discussion

Although some surgeons were skeptical about laparoscopic hepatectomy, it is now generally agreed to be a feasible option for left lateral section (segments 2 and 3) and non-anatomical resection of small tumours (<5 cm) in segments 4b, 5, and 6.[1,2,7] We adopted this guideline in selecting patients for laparoscopic liver resection, with the exception of one patient who had an exceptionally large pedunculated tumour (9 cm) that had arisen from the peripheral part of the left lateral section.

Of the laparoscopic instruments available, handports have been used by some surgeons to facilitate exposure, provide tactile palpation and allow immediate haemostasis if massive bleeding occurs.[11,12] However, the wound required for a handport seems to defeat the purpose of minimising the access trauma. Also the handport itself may block the field of dissection. As the majority of our specimens were small, they could be easily retrieved through extended port sites. Moreover, unlike other surgeons[7,12] we did not use the Pringle manoeuvre in our resections. This was because we were mindful that its routine application might cause ischaemic insult to the liver remnant, thus contributing to postoperative liver failure, particularly in cirrhotic patients. With the use of a meticulous technique to control blood loss, we found inflow vascular occlusion unnecessary.

For laparoscopic hepatectomies, we initially used CUSA in combination with the TissueLink de-

vice.[13] However, the laparoscopic CUSA probe slowed the progress of transection, and we soon switched to using LigaSure in combination with the TissueLink.[14] In one instance, we also tried radiofrequency-assisted liver resection, which turned out to be our only case with a grossly involved resection margin, and thus we applied RFA to the resection margin in the remnant liver. In line with other authors,[15] we also found endovascular staplers useful in controlling bleeding from the major vascular pedicle in the course of left lateral sectionectomy. These staplers also made the operation safer and faster.

Several other studies have compared laparoscopic and open liver resection.[16-21] As in our series, all of them revealed similar morbidity and mortality for the two approaches. Two studies have shown that laparoscopic resection takes longer,[16,19] but four others revealed no statistically significant difference in operation durations.[17,18,20,21] Individual studies have also shown that laparoscopic resection is associated with decreased blood loss,[19,20] and less need for analgesia,[17,18] earlier resumption of an oral diet,[17,21] and a shorter hospital stay.[16-18,20] Two studies addressed the issue of resection margins; both showed no difference between the laparoscopic and open groups.[18,20] Only one other study assessed the survival and disease-free survival of the two groups, and showed no statistically significant difference between the two groups.[21]

In our study, patient and tumour characteristics as well as pathological findings were adequately matched in the two groups. Further, as the same three surgeons operated on both groups during the same period, we eliminated biases related to individual surgeons and time of recruitment. With an acceptable conversion rate to an open procedure of 8%, the laparoscopic group yielded a low morbidity (4%) and zero mortality, as ensued in the open group. Importantly, the laparoscopic group had significantly less blood loss without significantly longer operating times. The exact reason for less blood loss associated with laparoscopic procedure is uncertain, but may be due to slower and more meticulous dissection under magnified view, decreased bleeding from hepatic vein tributaries due to pneumoperitoneum, less blood loss from the abdominal wound, and finally the more frequent use of vascular staplers. The other major benefits of the laparoscopic technique were less wound trauma and less recourse to postoperative analgesia, a shorter time needed to resume an oral diet and hastened discharge from hospital. The small wounds in the laparoscopic group (Fig 3) were not only cosmetically more desirable than those in the open group, but also resulted in less intra-abdominal adhesions, which could facilitate subsequent operations should the need arise.

The main drawbacks of our study were the relatively short overall follow-up period, and the longer follow-up period in the open resection group. The latter imbalance arose because we performed more laparoscopic resections in the later half of the study period. Nevertheless, there was no statistically significant difference between the actuarial and disease-free survivals in the two groups.

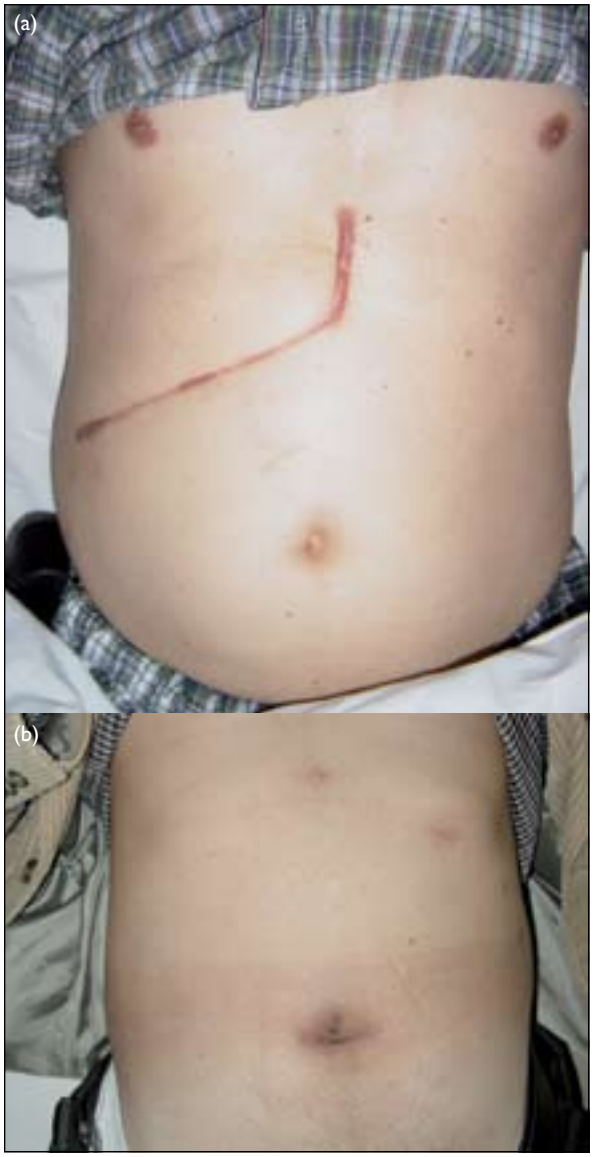


FIG 3. Scars after surgery for (a) open left lateral sectionectomy and (b) laparoscopic left lateral sectionectomy

Conclusion

We conclude that in selected patients, laparoscopic resection of liver tumours is not only feasible and safe, but also achieves less blood loss, less pain, earlier resumption of an oral diet, a shorter hospital stay, and a better cosmetic appearance. Contrary to the concerns of some surgeons, the laparoscopic approach does not compromise the resection margin. However, longer follow-up is required to

determine whether laparoscopic resection will affect long-term survival. From the findings of this study, malignancy itself should not be a contra-indication for laparoscopic liver resection.

References

1. Gagner M, Rogula T, Selzer D. Laparoscopic liver resection: benefits and controversies. Surg Clin North Am 2004;84:451-62.
2. Kaneko H. Laparoscopic hepatectomy: indications and outcomes. J Hepatobiliary Pancreat Surg 2005;12:438-43.
3. Gagner M, Rheault M, Dubuc J. Laparoscopic partial hepatectomy for liver tumor. Surg Endosc 1992;6:99.
4. Gigot JF, Glineur D, Santiago AJ, et al. Laparoscopic liver resection for malignant tumors: preliminary results of a multicenter European study. Ann Surg 2002;236:90-7.
5. Descottes B, Glineur D, Lachachi F, et al. Laparoscopic liver resections of benign liver tumors. Surg Endosc 2003;17:23-30.
6. Mala T, Edwin B, Rosseland AR, Gladhaug I, Fosse E, Mathisen O. Laparoscopic liver resection: experience of 53 procedures at a single center. J Hepatobiliary Pancreat Surg 2005;12:298-303.
7. Cherqui D, Laurent A, Tayar C, et al. Laparoscopic liver resection for peripheral hepatocellular carcinoma in patients with chronic liver disease: midterm results and perspectives. Ann Surg 2006; 243:499-506.
8. O'Rourke N, Fielding G. Laparoscopic right hepatectomy: surgical technique. J Gastrointest Surg 2004; 8:213-6.
9. Dulucq JL, Wintringer P, Stabilini C, Berticelli J, Mahajna A. Laparoscopic liver resection: a single center experience. Surg Endosc 2005;19:886-91.
10. Vibert E, Perniceni T, Levard H, Denet C, Shahri NK, Gayet B. Laparoscopic liver resection. Br J Surg 2006;93:67-72.
11. Inagaki H, Kurokawa T, Nonami T, Sakamoto J. Hand-assisted laparoscopic left lateral segmentectomy of the liver for hepatocellular carcinoma with cirrhosis. J Hepatobiliary Pancreat Surg 2003;10:295-8.
12. Tang CN, Tsui KK, Ha JP, Yang GP, Li MK. A single-centre experience of 40 laparoscopic liver resections. Hong Kong Med J 2006;12:419-25.
13. Di Carlo I, Barbagallo F, Toro A, Sofia M, Guastella T, Latteri F. Hepatic resections using a water-cooled, high density, monopolar device: a new technology for safer surgery. J Gastrointest Surg 2004;8:596-600.
14. Saiura A, Yamamoto J, Koga R, et al. Usefulness of LigaSure for liver resection: analysis by randomized clinical trial. Am J Surg 2006;192:41-5.
15. Belli G, Fantini C, D'Agostino A, Belli A, Cioffi L, Russolillo N. Laparoscopic left lateral hepatic lobectomy: a safer and faster technique. J Hepatobiliary Pancreat Surg 2006;13:149-54.
16. Rau HG, Buttler E, Meyer G, Schardey HM, Schildberg FW. Laparoscopic liver resection compared with conventional partial hepatectomy—a prospective analysis. Hepatogastroenterology 1998;45:2333-8.
17. Farges O, Jagot P, Kirstetter P, Marty J, Belghiti J. Prospective assessment of the safety and benefit of laparoscopic liver resections. J Hepatobiliary Pancreat Surg 2002;9:242-8.
18. Mala T, Edwin B, Gladhaug I, et al. A comparative study of the short-term outcome following open and laparoscopic liver resection of colorectal metastasis. Surg Endosc 2002;16:1059-63.
19. Lesurtel M, Cherqui D, Laurent A, Tayar C, Fagniez PL. Laparoscopic versus open left lateral hepatic lobectomy: a case-control study. J Am Coll Surg 2003;196:236-42.
20. Morino M, Morra I, Rosso E, Miglietta C, Garrone C. Laparoscopic vs open hepatic resection. A comparative study. Surg Endosc 2003;17:1914-18.
21. Kaneko H, Takagi S, Otsuka Y, et al. Laparoscopic liver resection of hepatocellular carcinoma. Am J Surg 2005;189:190-4.