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Pure Laparoscopic Hepatectomy for HCC Patients

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1. Introduction

Pure laparoscopic hepatectomy is thought to be a less invasive procedure than conventional open hepatectomy for the resection of hepatic lesions (1). Recent development of devices facilitates expansion of the indication of the procedure (2, 3). At the present moment, common advantages of laparoscopic surgery, such as early recovery and discharge with smaller postoperative pain and earlier intake, have been reported (4). However, specific advantages and/or disadvantages of pure laparoscopic hepatectomy for the settlement of the indication have yet to be sufficiently discussed.

On the other hand, at the treatment of hepatocellular carcinoma (HCC) with liver cirrhosis, considerations for the control of invasive surgical stress, especially to impaired liver, should be placed besides oncological therapeutic effects. Patients with severe liver cirrhosis have various (overt and preliminary) symptoms, such as 1) deteriorations of protein synthesis and metabolism, 2) congestion of GI tract, ascites, pancytopenia due to portal hypertension and hypersplenism, 3) susceptibility to infectious diseases and hepatopulmonary syndrome (hypoxaemia) due to increased shunt vessels (5). Cirrhotic patients have high morbidity and mortality at undergoing anesthesia and surgery (6) and the risk of abdominal operations increases according to the preoperative Child's class of the patients (7). Hepatic resection for severe cirrhotic patients, even minimum, often develops refractory ascites which leads to fatal complications (8, 9). In Japan, the criteria based on 3 parameters (the presence or absence of ascites, total serum billirubin level, and indocyanine green retension rate at 15 minutes (ICG R15)) have been widely used for patient selection of hepatectomy (10). Nowadays, surgical resection, local ablation therapy or transarterial chemoembolization is adapted to each HCC patient with liver cirrhosis depending on the tumor condition and the liver function.

However, not small number of HCC patients with severe liver dysfunction exists who is not able to undergo those treatment modalities due to liver function, tumor size and/or localization, especially after repeat treatments for the disease. Furthermore, not small portion of patients need the repeat treatments for multicentric metachronous lesions occurred in chronic impaired liver. For thosee patients, "less invasive" pure laparoscopic hepatectomy may provide a good option.

2. Pure laparoscopic hepatectomy for HCC patients with liver cirrhosis- our experiences

From May 2005, 21 patients with hepatocellular carcinoma and chronic liver disease underwent pure laparoscopic hepatectomy. There were 6 out of 21 patients had severe liver cirrhosis (Child-Pugh B/C and ICG R15 of 40% or above) (Table 1). These 6 patients and the other 14 patients (Child A and ICG R15: 10.1- 27.4 (median: 13.4) %, excluded the patient with HCC and rectal carcinoma) were compared in operating time, intraoperative blood loss, day of oral ingestion started, day of drain removal, total dose of drain discharge from the operation day to post operative day 3, complication, and postoperative hospital stay.

Age, Sex	Background liver disease	Child-Pugh (ICGR15 (%))	TB/DB (mg/dl)	PT (%)	Alb (g/dl)	Tumor location, Tumor size (mm)	Postoperative Complication
64, M	B,C	B (42.8%)	1.3/0.3	79	3.2	S4 and 2-3, 44	Cholecyctitis
53, M	B	B (41.2%)	1.5/0.4	75	3.4	S5-6, 28	no
68, F	C	C (58.2%)	2.2/0.5	58	2.6	S8, 13	no
40, M	Alc	B (52.5%)	1.7/0.4	74	2.8	S6-7, 20	no
50, M	C	C (48.9%)	2.1/1.0	66	2.7	S5, 18	no
75, F	C	B (42.5%)	1.3/0.8	63	3.2	S3, 30	no

Table 1. Patients with severe liver cirrhosis who underwent pure laparoscopic hepatectomy
B: type-B viral hepatitis, C: type-C viral hepatitis, Alc: alcoholic hepatitis

For 6 patients with HCC and severe liver cirrhosis who underwent pure laparoscopic hepatectomy, the operating time was 140-341 (median: 232) minutes (for other patients with mild/moderate liver cirrhosis: 216-528 (295) minutes), the intraoperative blood loss was uncountable-213 (median: 58) ml (for other patients with mild/moderate liver cirrhosis: uncountable -696 (43) ml), the day of oral ingestion started was postoperative day 1-3 (median: 2) (for other patients with mild/moderate liver cirrhosis: day 2-3 (2)), the day of drain removal was postoperative day 3-6 (median: 4) (for other patients with mild/moderate liver cirrhosis: day 4-6 (5)), the total dose of drain discharge from the operation day to post operative day 3 was 279-1990 (median: 820) ml (for other patients with mild/moderate liver cirrhosis: 141-1275 (416) ml), and the postoperative hospital stay was 11-21 (median: 17) days (for other patients with mild/moderate liver cirrhosis: 9-254 (20) days). One patient developed postoperative complication of cholecystitis among 6 patients with severe liver cirrhosis, and 2 patients developed postoperative complication of ileus and refractory ascites among other 14 patients. There was no post-operative mortality in both groups. These results of perioperative course were comparable without statistically significant difference in the two groups. Perioperative course of HCC patients with severe liver cirrhosis who underwent pure laparoscopic hepatectomy was favorable and comparable to that of the other HCC patients with mild/moderate liver cirrhosis. (A case is shown in figures 1-5)

Also, repeat pure laparoscopic hepatectomy (and combined treatments) for patients with liver cirrhosis and multicentric/metachronous HCCs was feasible and safe with advantage of less post-operative adhesion. (A case is shown in figures 6-10)

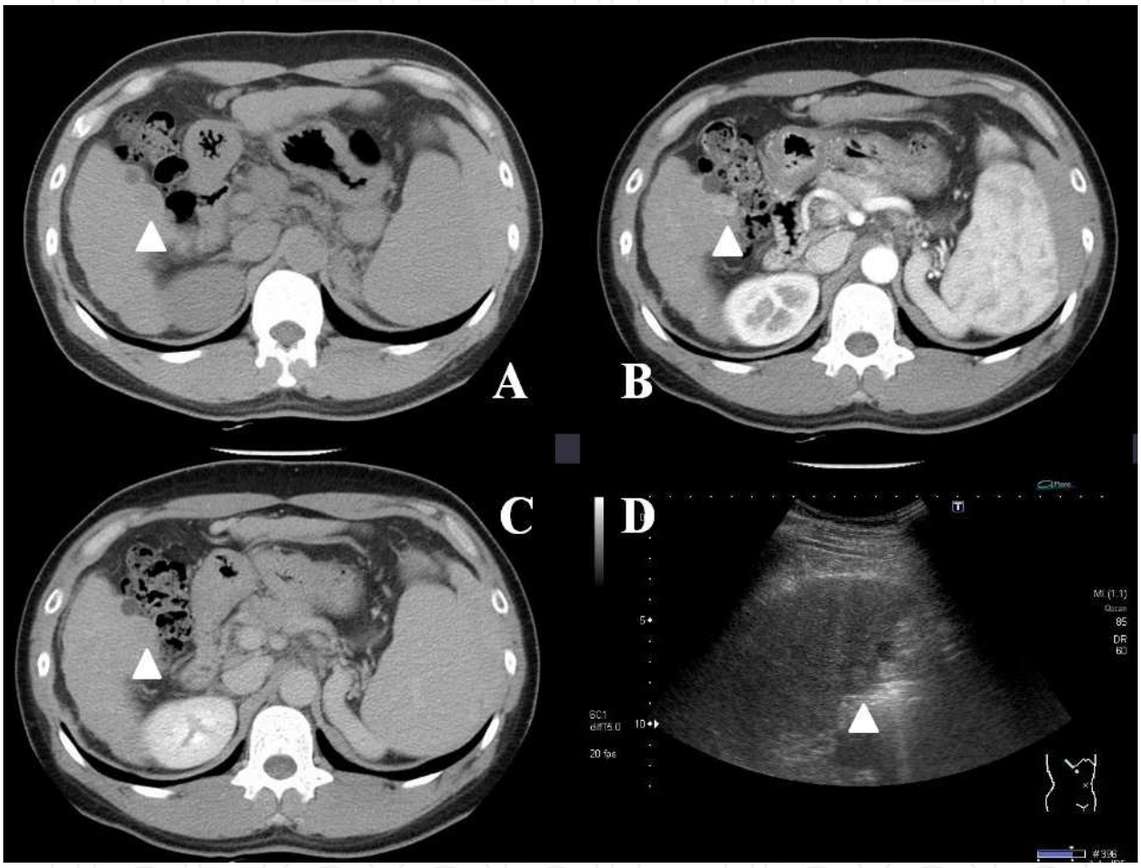

Fig. 1. A case with hepatocellular carcinoma and severe liver cirrhosis treated with pure laparoscopic hepatectomy
50 years old man with type-C severe liver cirrhosis (Table 1, patient 5) developed 2 cm hepatocellular carcinoma (HCC) at the undersurface area of the segments 5, revealed in computed tomography (plain (A), arterial phase with contrast (B), venous phase (C)) and ultrasonography (D).

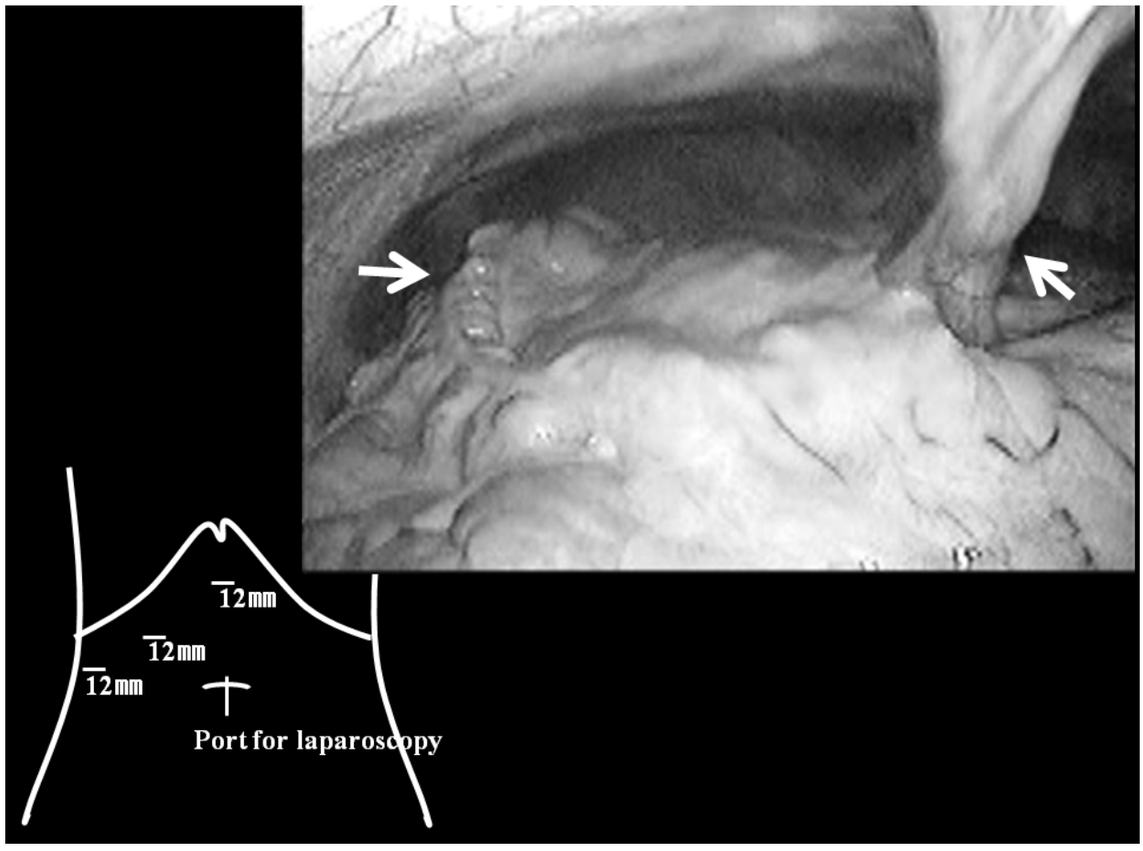

Fig. 2. Intraoperative findings of the case in figure 1 (1)
The liver was highly atrophic with large shunt vessels in the round ligament and the hepatic flexure of the colon was migrating into the subphrenic space.

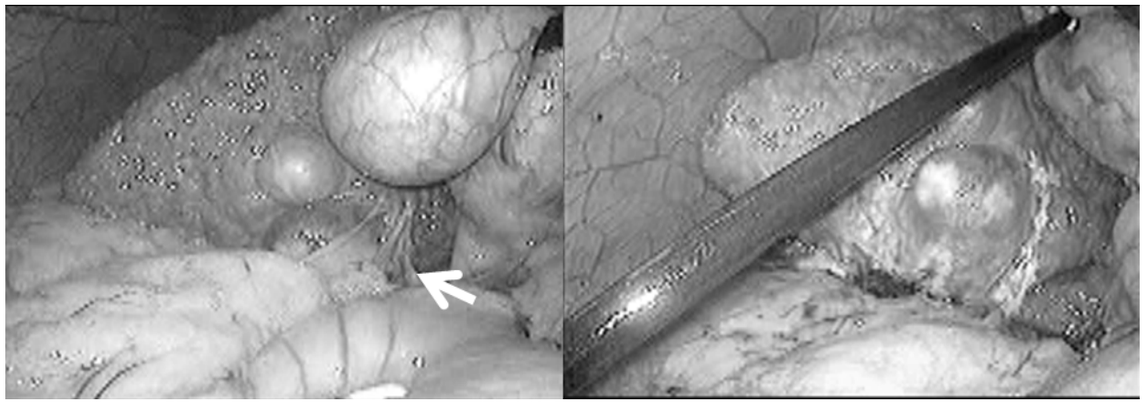

Fig. 3. Intraoperative findings of the case in figure 1 (2)
There were mild adhesions around the tumor. Dissection of the adhesion was performed, but not the mobilization of the liver. Since the liver was highly atrophic and the tumor was located deeply in the subphrenic space, mobilization of the liver was necessary for safe resection of the tumor under laparotomy. However, with laparoscopy, good direct vision and safe resection was obtained without mobilization.

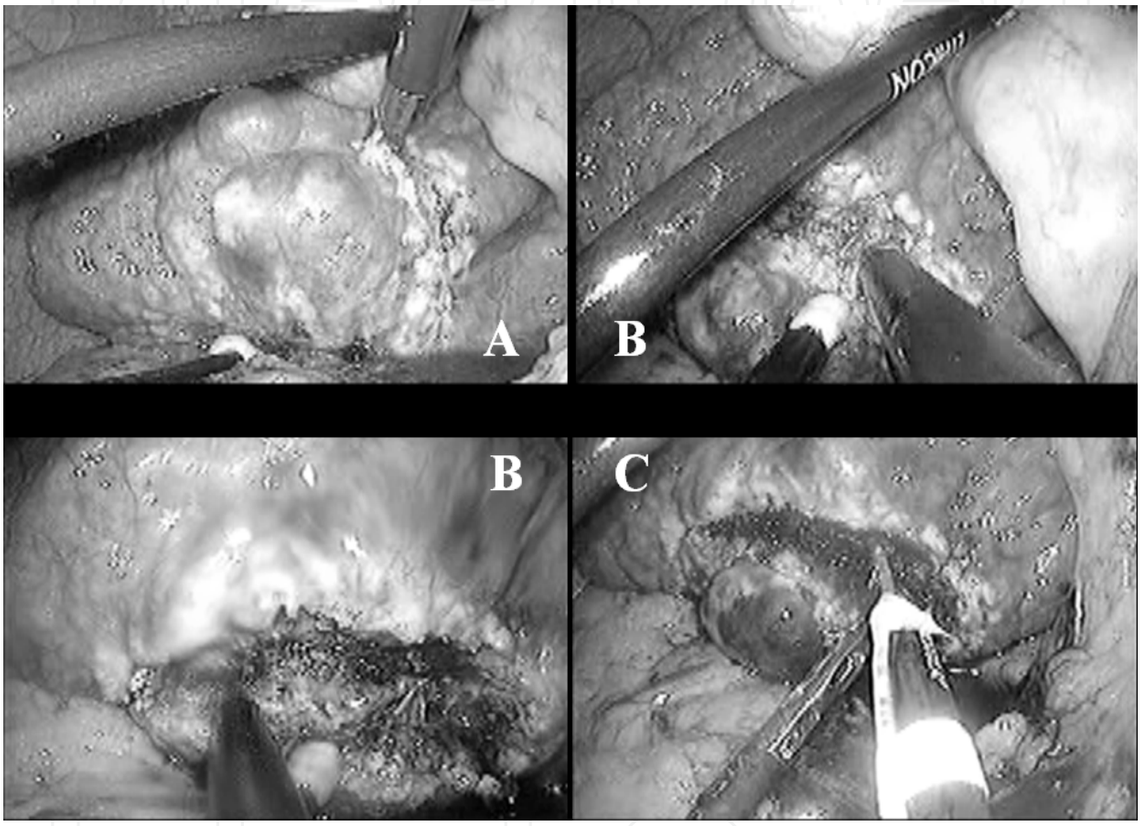

Fig. 4. Intraoperative findings of the case in figure 1 (3)
(A) After intraoperative ultrasonography, shallow cut in the surface area of the liver was made with harmonic scalpel.
(B) In the deeper area of the liver, dissection was performed with CUSA, monopolar and bipolar electric cautery. Thicker vessels were clipped or ligated and divided.
(C) The tissue with good coagulation with bipolar and monopolar was cut with scissors.

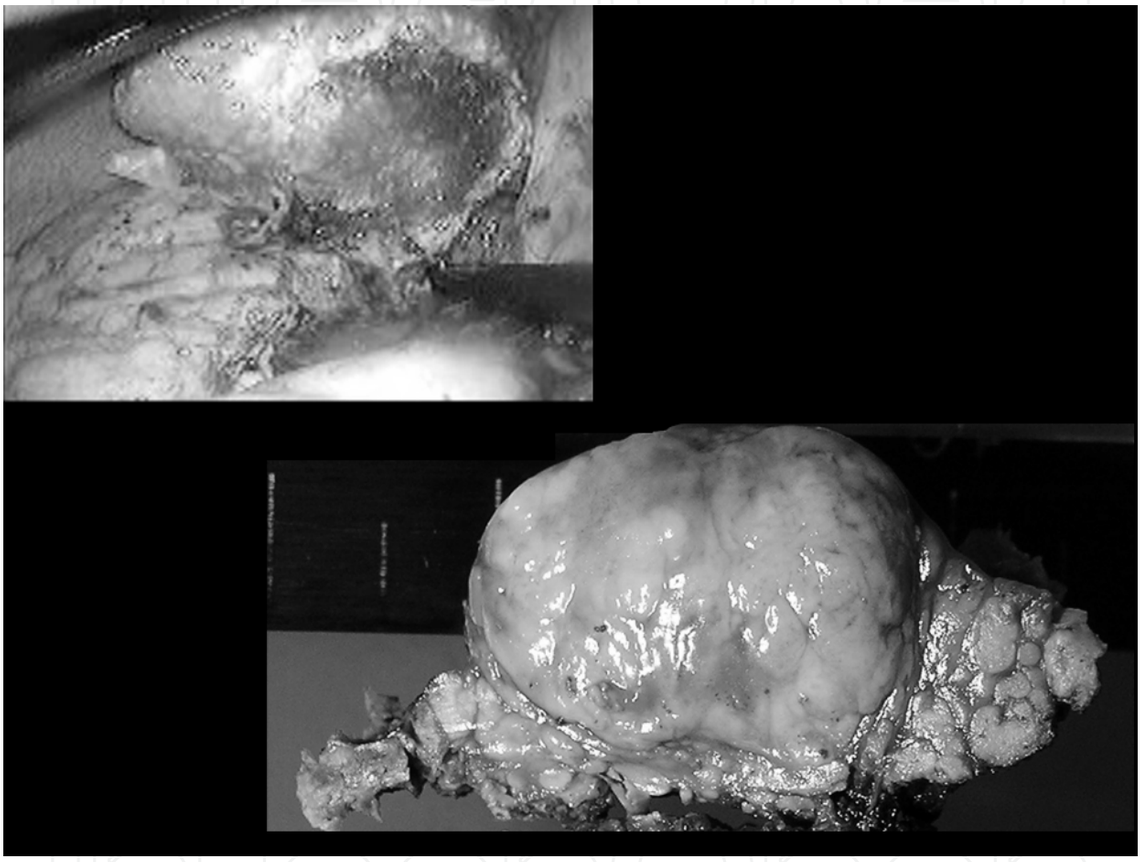

Fig. 5. Intraoperative findings (4) and resected specimen of the case in figure 1
The operation time was 140 minutes and intraoperative blood loss was 100ml. His post-operative hospital stay was uneventfull and 11 days. Pathologically, the tumor was moderately differentiated HCC in well differentiated HCC. He is alive without recurrence at 16 months after surgery

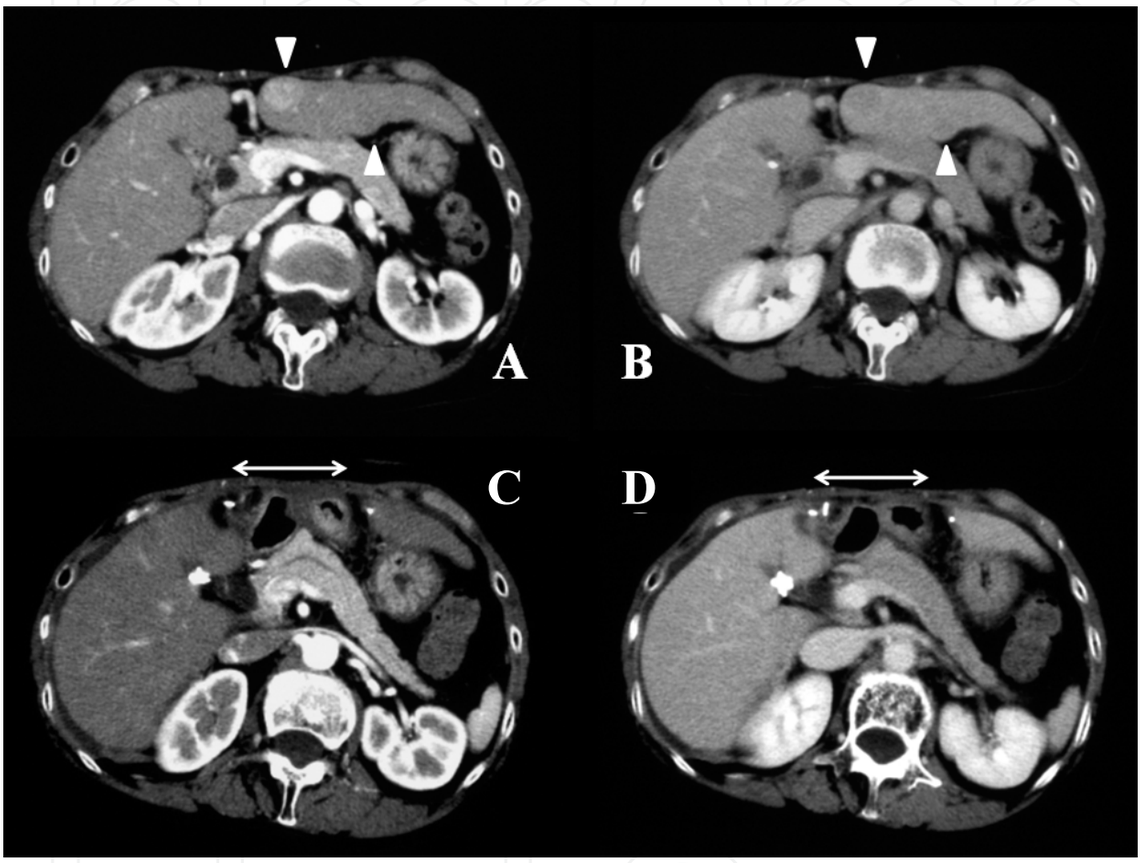

Fig. 6. A case with multicentric metachronous hepatocellular carcinomas and liver cirrhosis treated repeatedly with pure laparoscopic hepatectomy
69 years old woman with type-C liver cirrhosis developed 2 cm HCC in the segments 3 and 1.5cm in the border of segments 2 and 3, revealed in computed tomography (upper, arterial phase with contrast (A), venous phase (B)) and underwent pure laparoscopic hepatectomy (lower, arterial phase with contrast (C), venous phase (D)) in 2008. Pathological findings of the tumors were moderately (S3) and well (S2-3) differentiated hepatocellular carcinomas.

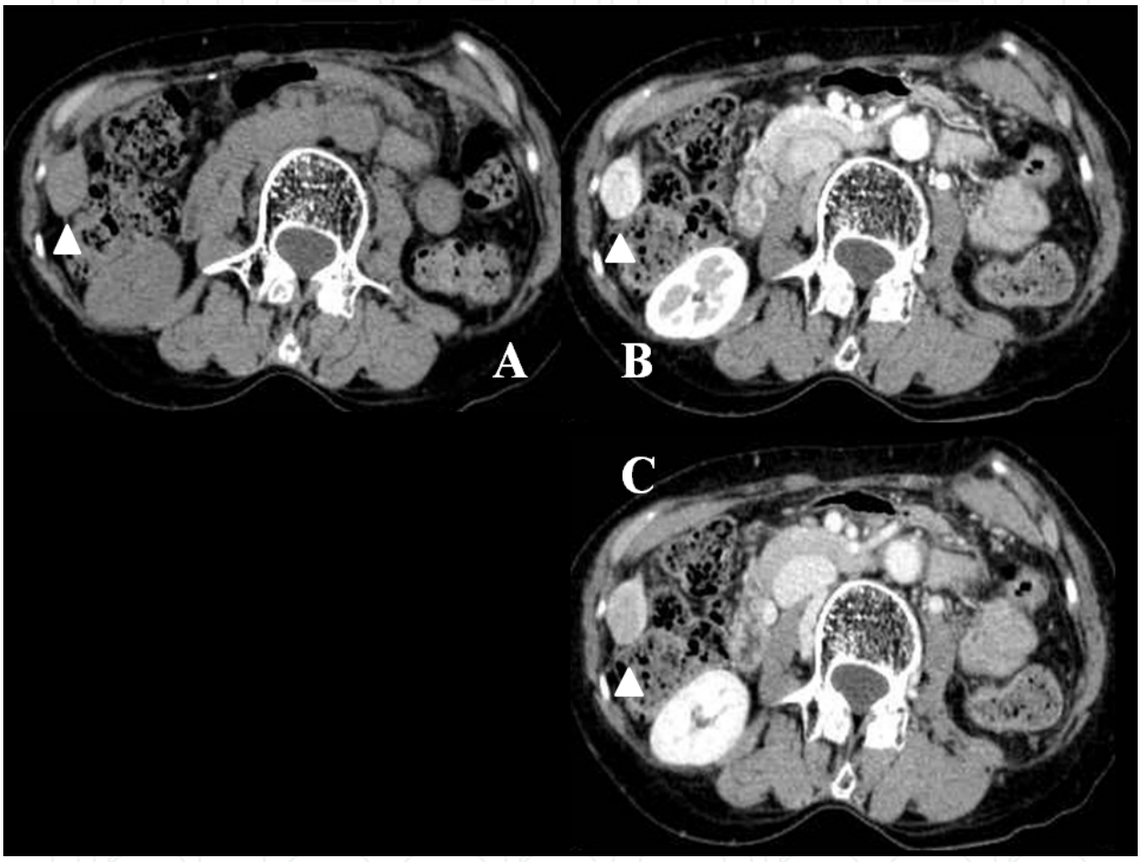

Fig. 7. A case with multicentric metachronous hepatocellular carcinomas and liver cirrhosis treated repeatedly with pure laparoscopic hepatectomy (2)
In 2010, she developed 2.5 cm HCC at the undersurface area of the segments 6, revealed in computed tomography (plain (A), arterial phase with contrast (B), venous phase (C)) and ultrasonography. She also had two small hypovascular lesions in the borders of segments 3 and 4, and of segments 4 and 8.

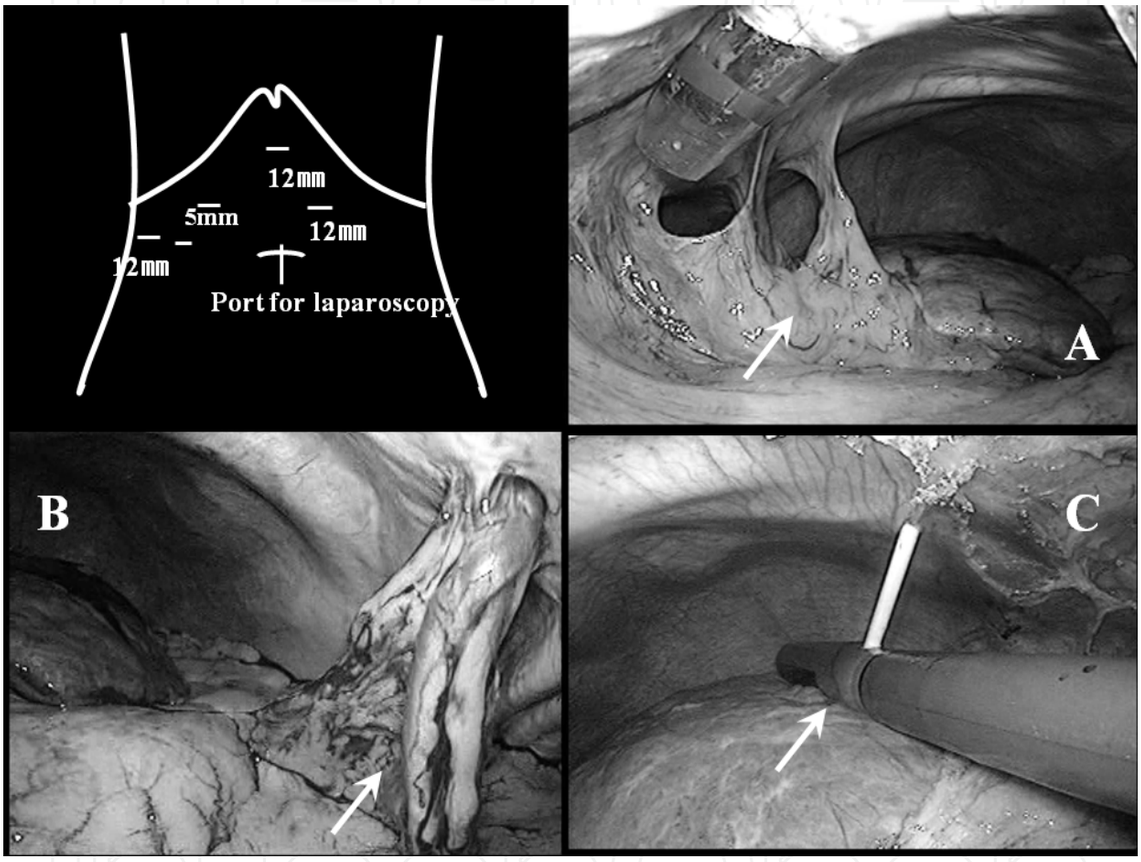

Fig. 8. Intraoperative findings of the case in figure 7 (1)
Adhesions were observed at the resected area of the liver (A) and the port site (B). There was shunt vessel formation in the port site adhesion. Two small hypovascular lesions in the borders of segments 3 and 4, and of segments 4 and 8 were ablated with US-guided intraoperative MCT (C).

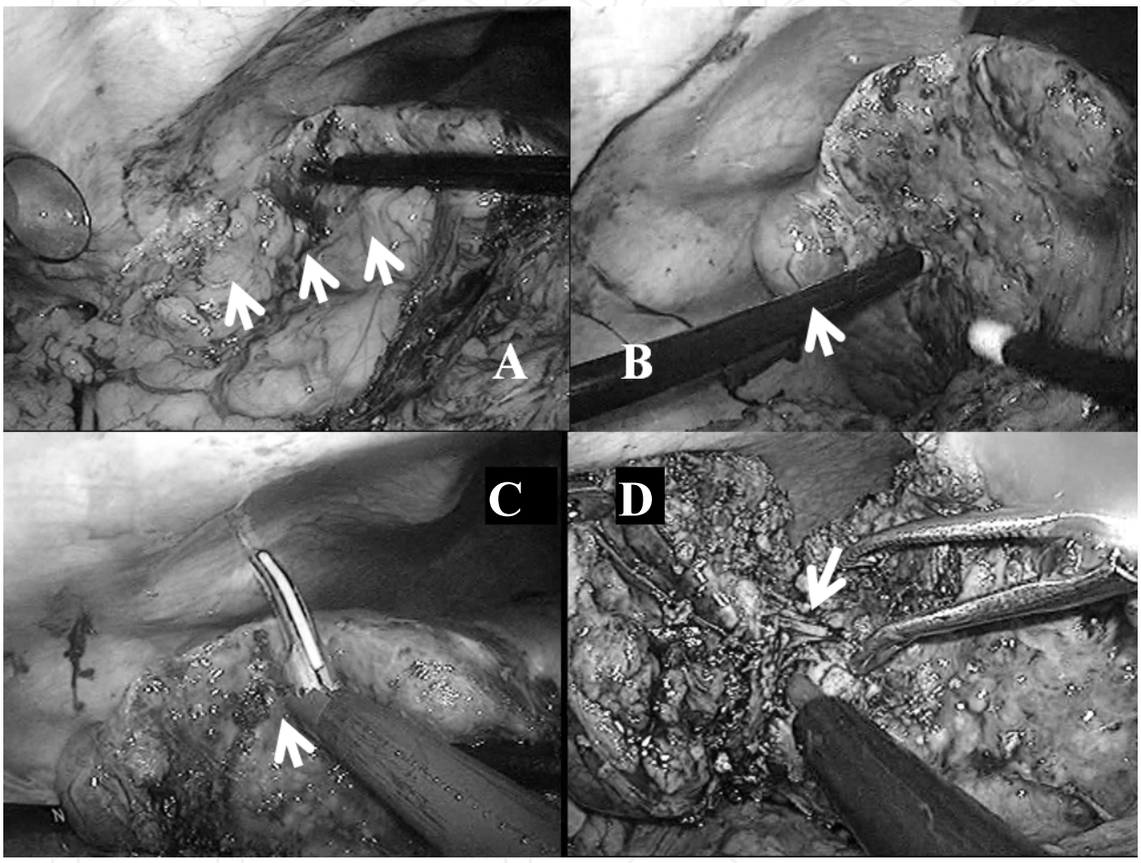

Fig. 9. Intraoperative findings of the case in figure 7 (2)
There were also adhesions at the undersurface area of the right lobe of the liver after laparoscopic cholecystectomy performed 8 years ago (A). Dissection of the adhesion, but not the mobilization of the liver, exposed the tumor (B). After intraoperative ultrasonography, shallow cut in the surface area of the liver was made with harmonic scalpel (C). In the deeper area of the liver, dissection was performed with CUSA, monopolar and bipolar electric cautery. Thicker vessels were clipped or ligated and divided (D).

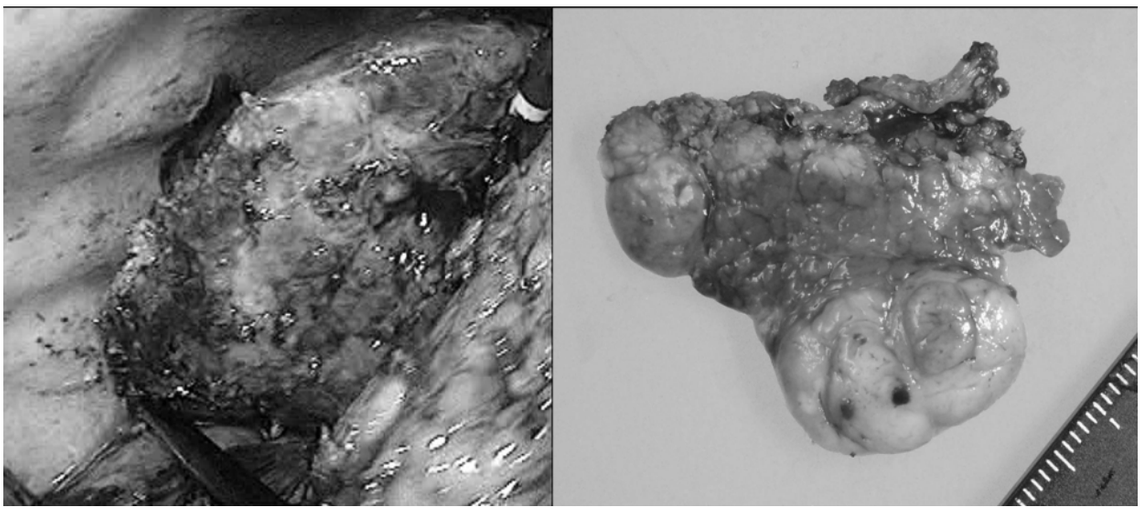

Fig. 10. Intraoperative findings of the case in figure 7 (3) and resected specimen of the case in figure

The operation time was 168 minutes and intraoperative blood loss was 30ml. Her post-operative hospital stay was uneventfull 9 days. Pathologically, the tumor was moderately differentiated HCC. She is alive without recurrence at 6 months after surgery

3. Discussion

Mirnezami et al recently reported systematic review and meta-analysis for short- and long-term outcomes after laparoscopic and open hepatic resection, with twenty-six studies met the inclusion criteria with a population of 1678 patients (60% of the patients had malignant liver tumor) (11). In their study, laparoscopic hepatectomy resulted in longer operating time, but reduced blood loss, portal clamp time, overall and liver-specific complications, and length of post-operative hospital stay. No difference was found between two groups for oncological outcomes. The benefits of laparoscopy may be particularly great for cirrhotic patients, given the potential for lower levels of parietal and hepatic injury and the preservation of venous and lymphatic collateral circulation. The safety and feasibility of the laparoscopic approach and its short-term benefits for HCC have been demonstrated by a few series to date (12-19). Tranchart et al recently reported laparoscopic resection of HCC for selected patients gave a better postoperative outcome without long- and short-term oncologic consequences from their series (42 each laparoscopic- and open-hepatectomy patients, with more than 96% Child A patients and mostly anatomical resection) (20). In our experience, perioperative course of 6 HCC patients with severe liver cirrhosis (Child B/C and ICG R15 of 40% or above) who underwent pure laparoscopic hepatectomy was favorable and comparable to that of the other HCC patients with mild/moderate liver cirrhosis.

Early postoperative recovery and discharge with smaller postoperative pain and earlier intake are advantages in pure laparoscopic hepatectomy for severe cirrhotic patients as the other laparoscopic surgery. On top of that, we consider that relatively small amount (median 230 ml/day) of drain discharge of severe liver cirrhosis patients, some (case 3, 5, 6 in table 1) of whom had mild or controllable ascites before surgery, was the other benefit of

pure laparoscopic hepatectomy for these patients in our series. Pure laparoscopic hepatectomy might have possible advantage of minimal postoperative drain discharge (ascites) which leads to lower risk of disturbance in water/electrolyte balance and hypoproteinemia. These disorders could trigger fatal liver failure. There are also reports which described little development of postoperative ascites on laparoscopic hepatectomy (14, 17). In case of pure laparoscopic hepatectomy for severe cirrhotic patients, this feature could be the most remarkable specific advantage for postoperative course. Patients who undergo hepatectomy are exposed three different types of stresses, 1) general surgical stress for whole body depends on operating time, amount of bleeding etc, 2) reduced liver function due to resected liver volume, 3) injury for liver parenchyma and environment around the liver by surgical procedure (destruction of the collateral blood and lymphatic flow caused by laparotomy and mobilization of the liver and, also, mesenchymal injury caused by compression of the liver). We consider that the reduction of the third type of stress mentioned above with pure laparoscopic hepatectomy leads to lowering the risk of refractory ascites, resulting in reduced risk of successive complications and smooth recovery for HCC patients with severe liver cirrhosis.

Liver surface HCC with severe liver cirrhosis is not the good candidate of percutaneous ablation therapy due to the concern about hemorrhage, tumor dissemination, and injury of adjacent organs. There are reports of microwave or radiofrequency ablation therapy under mini-laparotomy or laparoscopy for those tumors as safe and less invasive procedure (21). However, surgery should obtain better control for the tumor located in the surface area with minimum reduction of liver function, as Buell et al described (22). We think pure laparoscopic hepatectomy for those tumors with minimum invasiveness could be established as a feasible and more effective treatment modality. The tumor located deep in the liver with severe cirrhosis should be good candidate of percutaneous ablation therapy. The resection of the tumor located in the surface but bare area of the liver should need dissection of the attachments and mobilization of the liver. For these tumors, transpleural or retroperitoneal approach may need to be considered for reducing invasiveness. For the extension of the indication, hand-assisted laparoscopic hepatectomy with the incision for hand port in the lower abdomen (2), robotic hepatectomy (23), and single-incision laparoscopic hepatectomy (24) might be a good option as conventional pure laparoscopic hepatectomy, although further investigation is needed.

In conclusion, our experiences suggest that pure laparoscopic hepatectomy for HCC patients with severe liver cirrhosis has specific advantage of minimal postoperative ascite production which leads to lower risk of disturbance in water/electrolyte balance and hypoproteinemia. The procedure minimize destruction of the collateral blood and lymphatic flow caused by laparotomy and mobilization of the liver and, also, mesenchymal injury caused by compression of the liver. It restrains the complications, which lead to the postoperative serious liver failure, such as massive ascites. Severe cirrhotic patients with tumors on the surface of the liver, in case of difficult adaptation of percutaneous ablation therapy and/or local recurrence after repeat treatments, are the good candidates for this procesure. Furthermore, repeat pure laparoscopic hepatectomy (and combined treatments) for patients with liver cirrhosis and multicentric/metachronous HCCs was feasible and safe with advantage of less post-operative adhesion and the procedure could be good option of bridging therapy to liver transplantation for the patients with severe liver cirrhosis and small HCC.

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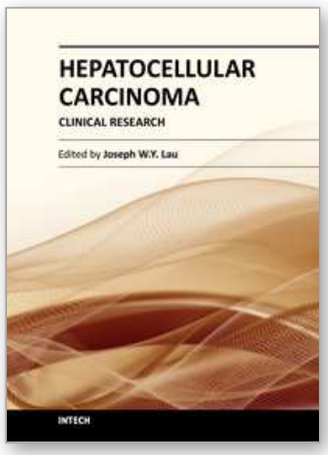

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This book covers the clinical aspects of hepatocellular carcinoma. This book is a compendium of papers written by experts from different parts of the world to present the most up-to-date knowledge on the clinical aspects of hepatocellular carcinoma. This book is divided into three sections: (I) Diagnosis / Differential Diagnosis; (II) Surgical Treatment; (III) Non-surgical Treatment. There are 19 chapters covering topics from novel diagnostic methods to hepatic lesions mimicking hepatocellular carcinoma, from laparoscopic liver resection to major hepatectomy without allogeneic blood transfusion, from molecular targeted therapy to transarterial radioembolization, and from local ablative therapy to regional therapy. This volume is an important contribution to the clinical management of patients with hepatocellular carcinoma. The intended readers of this book are clinicians who are interested in hepatocellular carcinoma, including hepatologists, liver surgeons, interventional and diagnostic radiologists, pathologists and epidemiologists. General surgeons, general physicians, trainees, hospital administrators, and instruments and drug manufacturers will also find this book useful as a reference.

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