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MINIREVIEWS

Pure laparoscopic hepatectomy for hepatocellular carcinoma with chronic liver disease

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Abstract

Pure laparoscopic hepatectomy is a less invasive procedure than conventional open hepatectomy for the resection of hepatic lesions. Increases in experiences with the technique, in combination with advances in technology, have promoted the popularity of pure laparoscopic hepatectomy. However, indications for usage and potential contraindications of the procedure remain unresolved. The characteristics and specific advantages of the procedure, especially for hepatocellular carcinoma (HCC) patients with chronic liver diseases, are reviewed and discussed in this paper. For cirrhotic patients with liver tumors, pure laparoscopic hepatectomy minimizes destruction of the collateral blood and lymphatic flow from laparotomy and mobilization, and mesenchymal injury from compression. Therefore, pure laparoscopic hepatectomy has the specific advantage of minimal postoperative ascites production that leads to lowering the risk of disturbance in water or electrolyte balance and hypoproteinemia. It minimizes complications that routinely trigger postoperative serious liver failure. Under adequate patient positioning and port arrangement, the partial resection of the liver in the area of subphrenic space, peri-inferior vena cava area or next to the attachment of retro-peritoneum is facilitated in pure laparoscopic surgery by providing good vision and manipulation in the small operative field. Furthermore, the features of reduced post-operative adhesion, good vision, and manipulation within the small area between the adhesions make this procedure safer in the context of repeat hepatectomy procedures. These improved features are especially advantageous for patients with liver cirrhosis and multicentric and/or metachronous HCCs.

Key words: Laparoscopic hepatectomy; Hepatocellular carcinoma; Liver cirrhosis; Chronic liver disease; Liver Tumor; Liver resection; Repeat hepatectomy; Bridging therapy to transplantation; Ascites; Postoperative liver failure

Core tip: For cirrhotic patients with liver tumor, pure laparoscopic hepatectomy minimizes destruction of the collateral blood/lymphatic flow from laparotomy and mobilization, and has advantage of minimal postoperative ascites. It restrains the complications, which trigger the postoperative liver failure. The partial resection in the area of subphrenic space, peri-inferior vena cava area or next to the attachment of retro-peritoneum is facilitated with good vision and manipulation in the small operative field. Furthermore, repeat pure laparoscopic hepatectomy for patients with multicentric/metachronous hepatocellular carcinomas was feasible and safe with the advantages of less post-operative adhesion and good vision and manipulation between the adhesions.

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INTRODUCTION

Since the first successful report of laparoscopic liver wedge resection in 1992[1], pure laparoscopic hepatectomy is thought to be a less invasive procedure than conventional open hepatectomy for the resection of hepatic lesions[2]. In a comprehensive meta-analysis study, laparoscopic hepatectomy was compared to open hepatic resection in 1678 patients across 26 studies. While it is associated with longer operating times and no differences in oncological outcomes, it is advantageous in several aspects[3]. Laparoscopic hepatectomy is associated reduced blood loss, decreased portal clamp time, a decrease in overall and liver-specific complications, and shorter postoperative hospital stays[3]. Recent technological development of devices and accumulation of experiences have facilitated the expansion of the indication of the procedure[4,5]. Common advantages of laparoscopic surgery, such as early recovery and discharge with smaller postoperative pain and earlier intake, have been reported also for laparoscopic hepatectomy[6]. However, specific advantages and/or disadvantages of pure laparoscopic hepatectomy for proper indication have not yet been resolved.

Hepatocellular carcinoma (HCC) is the fifth most common primary cancer and the third most common cause of cancer-related deaths worldwide[7,8]. The treatment options for HCC include surgical resection[9], liver transplantation[10], transarterial chemoembolization (TACE), and local ablation therapy[11]. Most experts think surgical resection and liver transplantation are the best hopes for cure. However, most patients with HCC have underlying chronic liver disease, and hence are at very high risk of developing significant postoperative complications. Although liver transplantation should be considered in patients with deteriorating liver function according to the Milan criteria[12], hepatic resection should be considered as a primary therapy in patients with well-preserved liver function[13,14]. When considering the treatment of HCC in patients with liver cirrhosis, the degree of invasive surgical stress, especially to the impaired liver, should be considered in addition to the oncological therapeutic effects. Patients with severe liver cirrhosis have various (overt and preliminary) symptoms, such as: (1) deteriorations of protein synthesis and metabolism; (2) GI tract congestion, ascites, pancytopenia due to portal hypertension and hypersplenism; and (3) susceptibility to infectious diseases and hepatopulmonary syndrome (hypoxaemia) due to increased shunt vessels[15]. Cirrhotic patients have high morbidity and mortality following anesthesia and surgery[16] and the risk of abdominal operations increases according to the preoperative Child-Pugh class of the patients[17]. Even limited resection following open surgery for severe cirrhotic patients often develops refractory ascites, which leads to fatal complications[18,19].

In Japan, criteria for selecting patient eligibility for hepatectomy is based on three parameters: (1) the presence or absence of ascites; (2) total serum bilirubin level; and (3) indocyanine green retention rate at 15 min (ICG R15)[20]. Currently, surgical resection, local ablation therapy, or TACE is adapted to each HCC patient with liver cirrhosis depending on the tumor condition and the liver function. However, a large number of HCC patients with severe liver dysfunction are not able to undergo those treatment modalities due to liver function, tumor size and/or localization. This is especially true after repeat treatments for the disease, including a large number of patients that need repeat treatments for multicentric metachronous lesions occurring in chronic impaired liver. For those patients, "less invasive" pure laparoscopic hepatectomy may provide a good option. The characteristics and advantages of pure laparoscopic hepatectomy for HCC patients with chronic liver diseases are discussed in this paper.

LAPAROSCOPIC HEPATECTOMY FOR HCC PATIENTS: AN OVERVIEW

The benefits of laparoscopic hepatectomy may be particularly advantageous 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 patients with chronic liver dysfunction have been demonstrated by several series[21-31]. To date, several studies have investigated the major differences between laparoscopic hepatectomy and open hepatectomy (Tables 1 and 2)[32-39]. Favorable short-term results, including fewer incidences of ascites and liver failure, and shorter postoperative hospital stays, correlate with the laparoscopic procedure. Tranchart *et al*[36] reported laparoscopic resection of HCC for selected patients resulted in better postoperative outcomes without long- and short-term oncologic consequences (42 each laparoscopic- and open-hepatectomy patients, with more than 96% Child-Pugh class A patients and mostly anatomical resection). Early postoperative recovery and discharge with less postoperative pain are usual advantages of laparoscopic surgery. Additionally, pure laparoscopic hepatectomy has the advantage of minimal ascites (Table 2), due to preservation of venous and lymphatic collateral circulation, which leads to lower risk of disturbance in water and/or electrolyte balance and hypoproteinemia, disorders that could trigger fatal liver failure. 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, whole-body surgical stress; (2) reduced liver function due to resected liver volume; and (3) surgery-induced injury for liver pa-

Table 1 Recently reported laparoscopic hepatectomy and open hepatectomy comparative studies - general information.

Ref.	No. of cases		Sex (male:female)		Age (yr, mean ± SD)		Background liver % of LC		Tumor size (cm, mean ± SD)		Type of resection nonanatomical:LLS: Anatomical	
	LH	OH	LH	OH	LH	OH	LH	OH	LH	OH	LH	OH
Laurent *et al*[32]	13	14	10:3	10:4	62.6 ± 9.5	65.9 ± 5.5	NA	NA	3.35 ± 0.89	3.43 ± 1.05	0:3:10	0:4:10
Belli *et al*[33]	23	23	10:13	14:9	59.5 ± 6.84	62.4 ± 7.7	100.00	100.0	3.10 ± 0.70	3.24 ± 0.70	0:5:18	0:6:17
Lai *et al*[34]	25	33	18:7	21:12	59 (35-79)[1]	59.0 (38-77)[1]	92.00	93.9	2.50 (1-7)[1]	2.60 (1-8)[1]	0:6:19	0:2:31
Aldrighetti *et al*[35]	16	16	11:5	12:4	65 ± 10	71.0 ± 6.00	56.30	56.3	4.00 ± 2.20	4.60 ± 2.50	0:5:11	0:5:11
Tranchart *et al*[36]	42	42	15:27	14:28	63.7 ± 13.10	65.7 ± 7.10	73.80	80.9	3.58 ± 1.75	3.68 ± 2.09	0:9:33	0:7:35
Kim *et al*[37]	26	29	18:8	20:9	57.84 ± 9.66	57.08 ± 9.78	NA	NA	3.15 (1-8)[1]	3.60 (1-19)[1]	0:4:22	0:3:26
Lee *et al*[38]	33	50	24:9	40:10	59 (36-85)[1]	58.50 (32-81)[1]	84.80	64.0	2.50 (1.5-9.0)[1]	2.90 (1.2-9.0)[1]	15:18:0	40:10:0
Truant *et al*[39]	36	53	31:5	47:6	60.6 ± 10.20	63.30 ± 7.60	NA	NA	2.90 ± 1.20	3.1 ± 1.20	0:22:14	0:26:27

[1]Expressed as median (range). LLS: Left lateral sectionectomy; LC: Liver cirrhosis; NA: Not available; LH: Laparoscopic hepatectomy; OH: Open hepatectomy.

Table 2 Recently reported laparoscopic hepatectomy and open hepatectomy comparative studies - operative outcomes

Ref.	Ascites		Liver failure		Hospital stay (d, mean ± SD)		Mortality	
	LH	OH	LH	OH	LH	OH	LH	OH
Laurent *et al*[32]	1/13	5/14	1/13	5/14	15.3 ± 8.6	17.3 ± 18.9	0/13	2/14
Belli *et al*[33]	3/23	8/23	NA	NA	8.2 ± 2.6	12.04 ± 3.93	1/23	0/23
Lai *et al*[34]	NA	NA	NA	NA	NA	NA	0/25	1/33
Aldrighetti *et al*[35]	0/16	1/16	NA	NA	6.3 ± 1.7	9.0 ± 3.8	0/16	0/16
Tranchart *et al*[36]	3/42	11/42	0/36	4/53	6.7 ± 5.9	9.6 ± 3.4	1/42	1/42
Kim *et al*[37]	0/26	1/29	NA	NA	11.08 ± 4.96	16.07 ± 10.697	0/26	0/29
Lee *et al*[38]	0/33	2/50	NA	NA	NA	NA	0/33	0/50
Truant *et al*[39]	5/36	12/53	NA	NA	6.5 ± 2.7	9.50 ± 4.8	0/36	4/53

LH: Laparoscopic hepatectomy; OH: Open hepatectomy; NA: Not available.

Table 3 Perioperative course after pure laparoscopic hepatectomy

	Cases with severe cirrhosis (n = 7) (ICG R15: ⩾ 40%, Child-Pugh B/C)	Cases with mild-moderate cirrhosis (n = 30)[1] [ICG R15: 8.7%-31.1% (median 13.2%), Child-Pugh A]
Operating time (min)	140-341 (232)	130-710 (302)
Intraoperative blood loss (mL)	NC-2750 (100)	NC-2400 (100)
Day of initiation of oral intake in POD	1/3 (2)	1-3 (2)
Drain discharge (as total of 0-3 POD, mL)	279-1990 (919)	60-3350 (416)
Postoperative hospital stay (d)	11/21 (17)	8-254 (18)
Morbidity	14.3% (Choleocystitis)	13.3% (Ileus, refractory ascites, bile leakage)
Mortality	0%	0%

[1]Excluded patients with combined surgery. NC: Not countable; POD: Post-operative day; ICG R15: Indocyanine green retention rate at 15 min.

renchyma and environment around the liver caused by destruction of the collateral blood and lymphatic flow by laparotomy and mobilization of the liver and mesenchymal injury caused by compression of the liver. Reduction of surgery-induced injury with pure laparoscopic hepatectomy lowers the risk of refractory ascites, resulting in reduced risk of successive complications and smooth recovery for HCC patients with severe liver cirrhosis.

We also experienced that the perioperative course of HCC patients with severe liver cirrhosis (Child-Pugh class B/C and ICG R15 of ⩾ 40%) who underwent pure laparoscopic hepatectomy was favorable and comparable to that of the other HCC patients with mild/moderate liver cirrhosis[40]. As of 2012, 40 patients with HCC and chronic liver disease underwent pure laparoscopic hepatectomy in our hospital. Seven out of 40 patients had severe liver cirrhosis (Child-Pugh class B/C and ICG R15 of ⩾ 40%). These seven patients and 30 other patients (Child-Pugh class A and ICG R15 of 10.1%-27.4%; three patients were excluded from analysis because of concomitant combined surgery) were compared in perioperative course (Table 3). The perioperative course results, such as intraoperative blood loss, day oral ingestion started, total dose of drain discharge to post operative day 3, morbidity and mortality, were comparable without statistically significant difference in the two groups. Among these seven patients, one underwent living-related liver transplantation 20 mo after hepatectomy.

This extensive review of the literature in combination with our clinical experiences indicate that pure laparo-

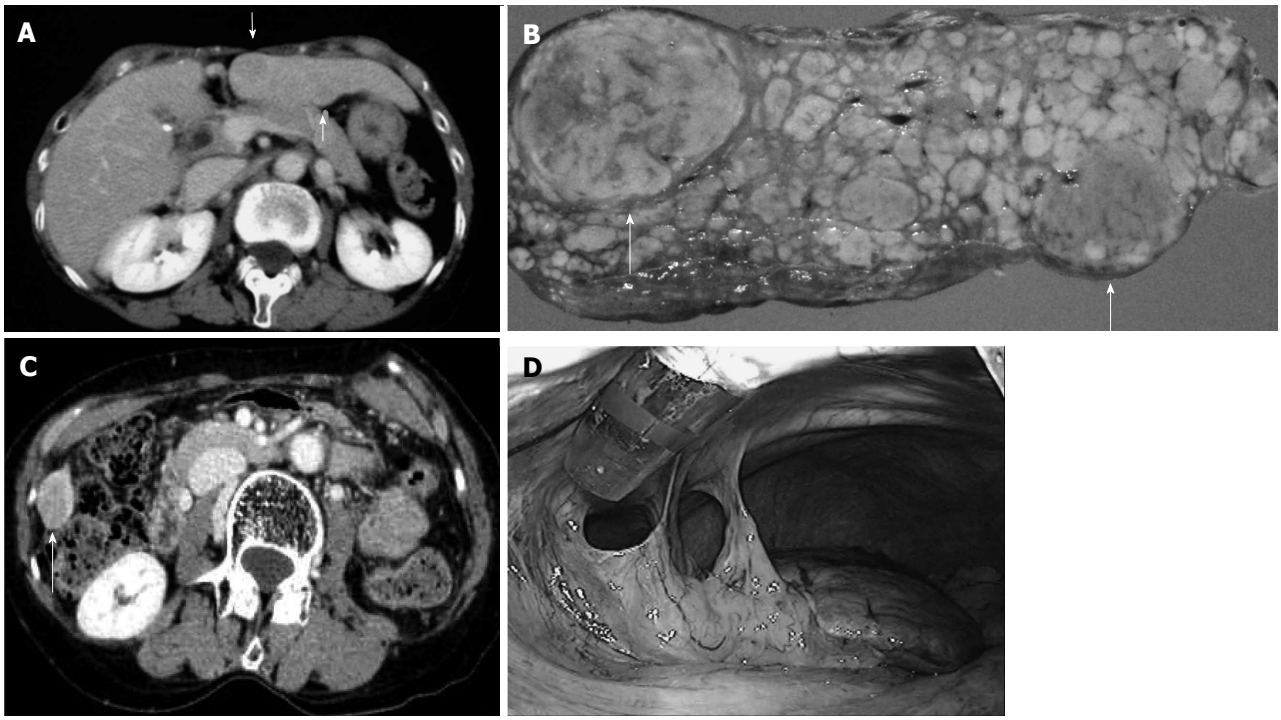

Figure 1 Repeat pure laparoscopic hepatectomy for patients with liver cirrhosis and hepatocellular carcinomas was feasible and safe: case 1. A: Computed tomorgraphy scan shows two hepatocellular carcinomas (HCC) in segment 3; B: The tumors (arrows) resected laparoscopycally.; C: A 69-year-old woman with type-C liver cirrhosis developed a new HCC on the caudal edge of segment 6 of the liver 2 years after the first hepatectomy; D: At the second laparoscopic hepatectomy, there was only mild adhesion around the resected area

scopic hepatectomy is the better therapeutic option for 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. The procedure may also prove to be an advantageous option in bridging therapy to liver transplantation for HCC patients with severe liver cirrhosis.

LAPAROSCOPIC HEPATECTOMY FOR HCC PATIENTS: ADVANTAGES AND DISADVANTAGES

At the introduction of laparoscopic hepatectomy in 1997, we selected the patients who could undergo adequate oncological pure laparoscopic resection for cancers. The indication of pure laparoscopic hepatectomy had been gradually extended from liver surface partial resection to large anatomical resection (right hepatectomy and posterior/anterior sectionectomy). The inclusion criteria are now a tumor size less than 10 cm without severe adhesion, invasion to major vessels, or a need for reconstruction of vessels or biliary tract.

As of 2012, we have performed forty of pure laparoscopic hepatectomy for HCC with chronic liver diseases, including ten cases of anatomical resections and four cases of repeat hepatectomy. There was no operative-mortality and the rate of morbidity was 12.5%. Tumor numbers are 1-4 and sizes are 1.1-7.8 cm. The median of their operating time and blood loss was 288 min and 50 mL. From these experiences, we propose the following advantages of laparoscopic hepatectomy for HCC patients: (1) advantageous for repeat procedures: Repeat pure laparoscopic hepatectomy (and combined treatments) for patients with liver cirrhosis and multicentric/metachronous HCCs was feasible and safe. The procedure also resulted in less post-operative adhesion and good vision and manipulation in the small area between the adhesions (case 1, Figures 1 and 2); (2) minimal invasion due to good vision: With adequate port arrangement and positioning of the patients[41,42], the manipulation in the small operative field is facilitated by good vision of the peri-inferior vena cava (IVC) area, subphrenic space, the area next to the attachment of retro-peritoneum, and the area between the adhesions. Therefore, there is a minimum need for dissection and/or adhesiolysis that could cause destructions of the collateral blood and lymphatic flows (case 2, Figures 3 and 4; case 3, Figures 5 and 6); and (3) better control of bleeding: Instead of compression and elevation of the bleeding field, other techniques are employed. These include meticulous manipulation under magnifying view, pressure control of pneumo-peritoneum and IVC, and various coagulating devices[43]. The ability of bleeding control is becoming matched to open surgery and anatomical hepatectomies with the exposure of major vessels recently becoming feasible[41,44-48].

The major disadvantages of laparoscopic surgery are in compression of the bleeding point, palpitation of

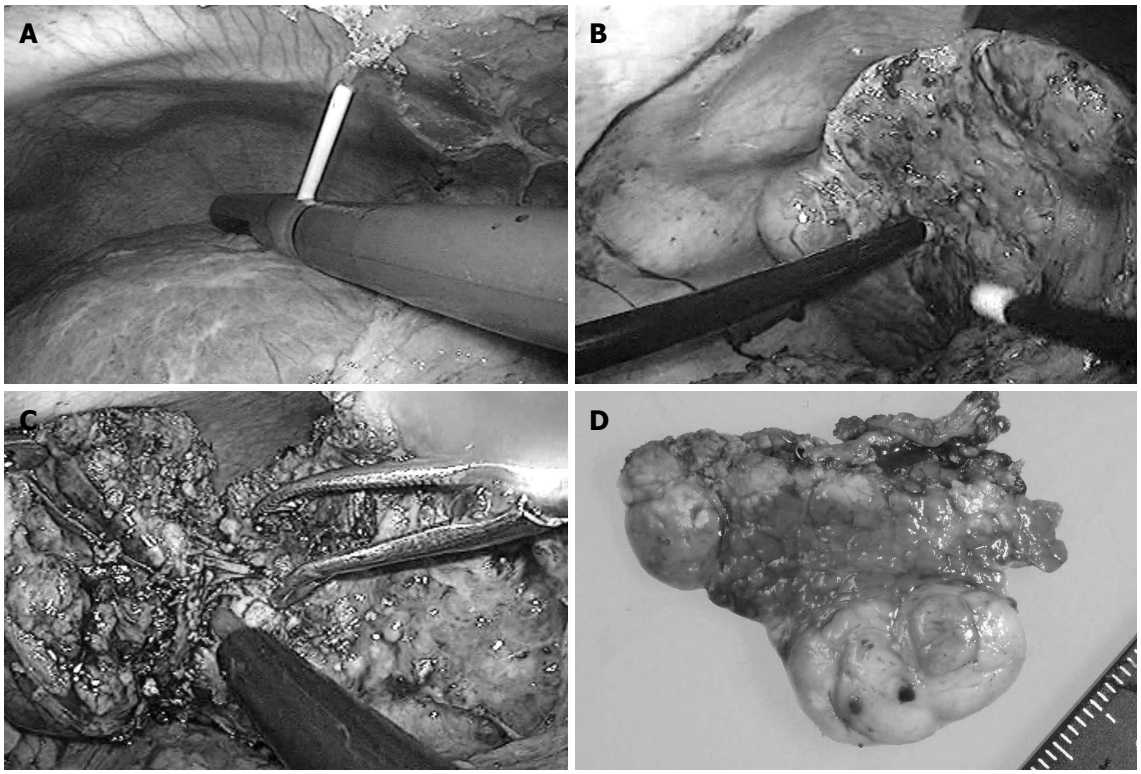

Figure 2 Repeat pure laparoscopic hepatectomy for patients with liver cirrhosis and hepatocellular carcinomas was feasible and safe: case 1. The patient also had two early lesions in segment four, which was treated with laparoscopic microwave coagulation therapy (A). After ablation therapy, the hepatocellular carcinomas (HCC) in segment 6 (B) was resected laparoscopically (C). The resected specimen (D) showed a single nodular HCC. The patient also underwent third hepatectomy for the lesion in segment one next to right adrenal gland two years after this operation.

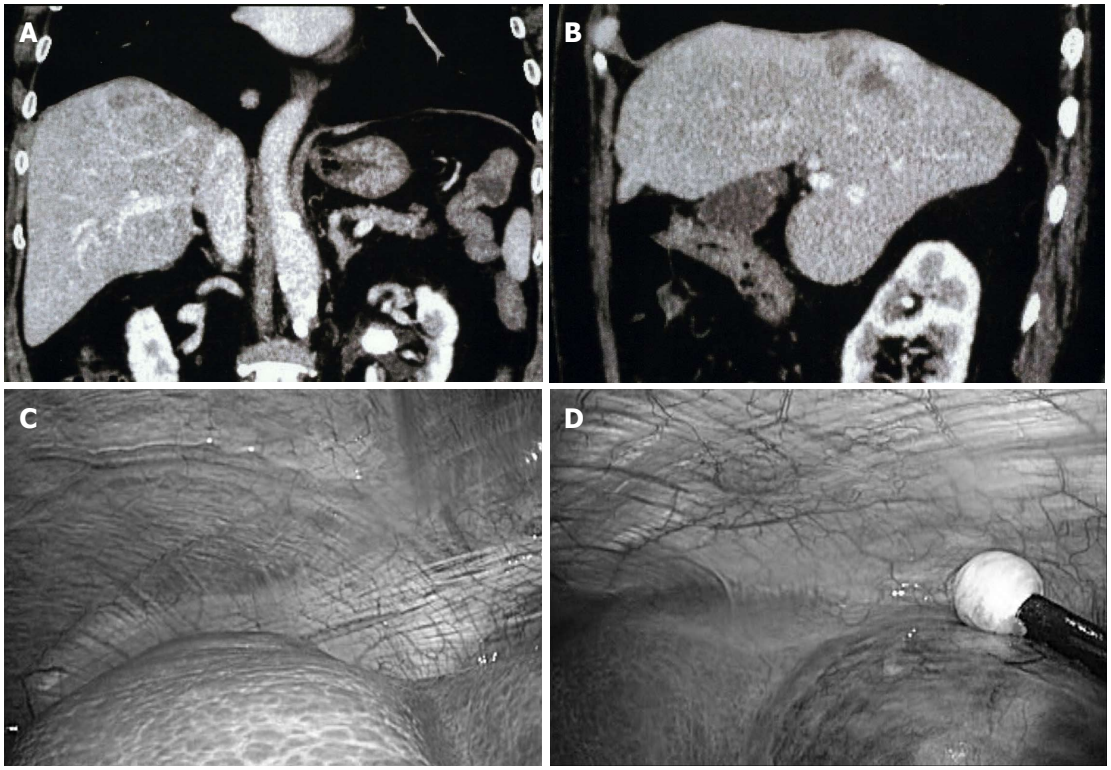

Figure 3 Pure laparoscopic hepatectomy is efficient in the subphrenic space: case 2. An 80-year-old woman with liver cirrhosis developed a hepatocellular carcinomas in the dorsal area of subsegment 8c of the liver revealed in computed tomography examination (A and B). Since the tumor compressed the right hepatic vein and her liver function seemed not to tolerate right hepatectomy or extended anterior sectionectomy, she underwent partial resection of the liver with the dissection and exposure of right hepatic vein and tumor capsule in pure laparoscopic hepatectomy. The tumor was located deeply in the subphrenic space (C) just next to the attachment of retro-peritoneum (D).

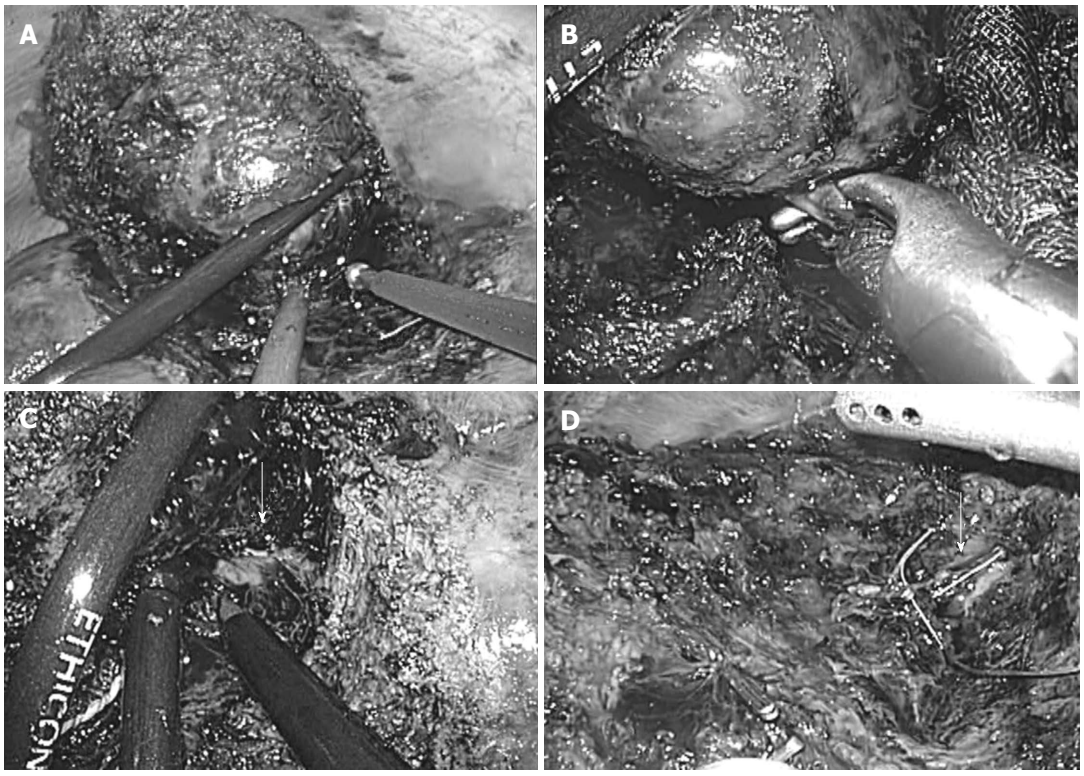

Figure 4 Pure laparoscopic hepatectomy is efficient in the subphrenic space: case 2. A: Resection of the tumor with the exposure of the capsule; B: Encircling and dividing of the direct branch of the right hepatic vein; C: Exposure of right hepatic vein; D: Cutting surface after resection.

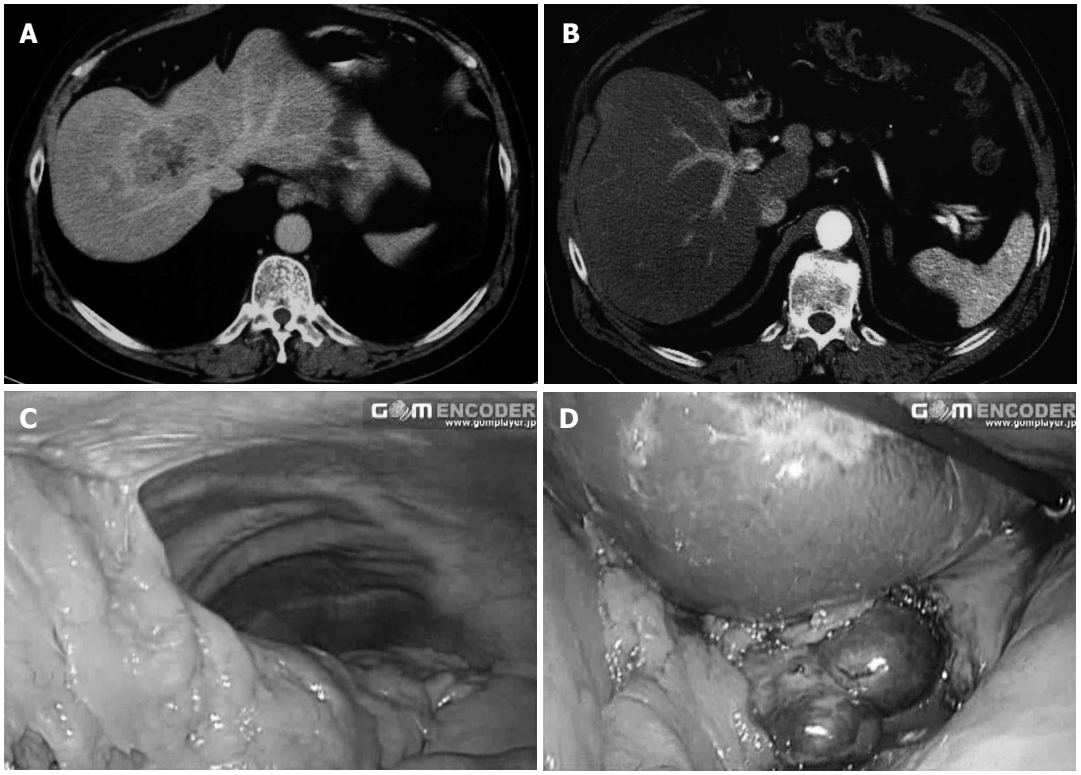

Figure 5 Pure laparoscopic hepatectomy is efficient between the adhesions and the peri-inferior vena cava area: case 3. Two years after a central bisectionectomy for hepatocellular carcinomas (HCC) at the roots of hepatic veins (A), a 66-year-old man developed a new prominent HCC on the left caudate lobe of the liver (B). Following the second pure laparoscopic hepatectomy, there was massive adhesion in the area of right upper abdomen (C). However, good view and access to the tumor were obtained with the dissection of omentum minus (D).

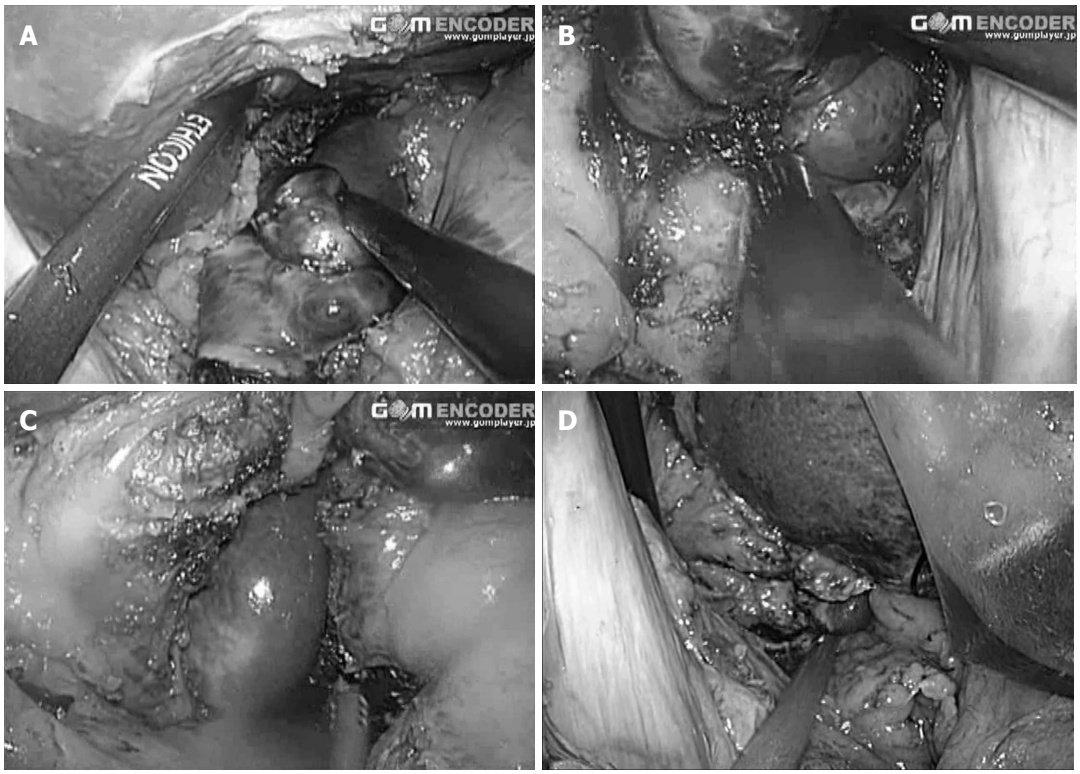

Figure 6 Pure laparoscopic hepatectomy is efficient between the adhesions and the peri-inferior vena cava area: case 3. A and B: Resection of the tumor; C and D: The view after the resection of the tumor.

the tumor, and overview of the whole abdominal fields. However, the advantages we have outlined above indicate that pure laparoscopic surgery should be chosen over open surgery for liver resection under specific conditions.

CONCLUSION

For cirrhotic patients with liver tumors, pure laparoscopic hepatectomy minimizes destruction of the collateral blood and lymphatic flow from laparotomy and mobilization, and mesenchymal injury from compression. Therefore, pure laparoscopic hepatectomy results in minimal postoperative ascites production, which leads to a lower risk of disturbance in water and/or electrolyte balance and hypoproteinemia. It leads to lower complications that could potentially lead to postoperative serious liver failure. These characteristics lead to facilitation of surgical treatments for such patients. Pure laparoscopic hepatectomy also results in improved vision and manipulation in a small operative field under the proper conditions. Further, in cases where it is necessary to perform repeat pure laparoscopic hepatectomy procedures, as well as combined treatments, pure laparoscopic hepatectomy proved to be safer. Finally, there is a minimum need for dissection and/or adhesiolysis which may cause perturbations in the collateral blood and lymphatic flows. These characteristics of pure laparoscopic hepatectomy indicate it is a superior method when compared to open hepatectomy under certain conditions.

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