



Original Article

Previous nonhepatectomy abdominal surgery did not increase the difficulty in laparoscopic hepatectomy for hepatocellular carcinoma: A case-control study in 100 consecutive patients

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ABSTRACT

Objectives: Laparoscopic hepatectomy (LH) is still technically challenging for patients with previous nonhepatectomy abdominal surgery (AS). Therefore, this study aimed to assess the difficulty of performing LH for patients with hepatocellular carcinoma (HCC) and a history of nonhepatectomy AS during the initial developing period of LH. **Materials and Methods:** The retrospective study enrolled patients who were newly diagnosed with HCC receiving LH from January 2013 to June 2021. Demographic characteristics, perioperative variables, and surgical complications were prospectively collected. **Results:** One hundred patients were reviewed consecutively, comprising 23 in the AS group and 77 in the non-AS group. No significant differences were observed in median IWATE score (5 vs. 5, $P = 0.194$), operative time (219 vs. 200 min, $P = 0.609$), blood loss (100.0 vs. 200.0 mL, $P = 0.734$), transfusion rate (4.3% vs. 10.4%, $P = 0.374$), duration of parenchyma transection (90.0 vs. 72.4 min, $P = 0.673$), and mean nonparenchymal transection time (191.0 vs. 125.0 min, $P = 0.228$), without increasing the conversion rate (0.0% vs. 3.9%, $P = 0.336$), postoperative complications (30.3% vs. 33.8%, $P = 0.488$), and postoperative hospital stay (6 vs. 7 days, $P = 0.060$) in AS group and non-AS groups. **Conclusion:** History of previous nonhepatectomy AS can lead to longer nonparenchymal transection time instead of conversion and did not increase the difficulty. Prolonged nonparenchymal transection time did not increase the surgical complications, prolong the postoperative hospital stay, and compromise the survival outcomes.

KEYWORDS: Abdomen/surgery, hepatectomy, laparoscopy, operative time, outcome

INTRODUCTION

Hepatocellular carcinoma (HCC) was ranked as the sixth most common neoplasm and the third leading cause of cancer death worldwide in 2020 with 905,677 diagnosed cases and 830,180 deaths [1]. Surgical resection is an effective treatment for lesions limited to an acceptable condition and well-preserved liver function under the suggestion of Barcelona Clinic Liver Cancer strategy [2]. Traditionally, open hepatectomy for liver malignancy is a common surgical procedure, especially in Asian countries. In the past 20 years, laparoscopic hepatectomy (LH) has been gradually performed in liver surgery. Although several favorable results of LH have emerged [3-5], this approach has still not been widely developed, especially in patients with a history of various abdominal surgeries.

Some reasons that may explain why LH is not widely accepted in earlier decades are as follows [6]: difficulty


in approaching the posterosuperior lesions, vascular control, inability to perform manual compression or suture for the bleeding, working with the deep intrahepatic areas, and intraoperative hazards, such as gas embolism, massive bleeding, and bile duct injury [7,8]. Moreover, in patients with a history of upper abdominal surgery (AS), postoperative changes such as adhesions at the liver surface and hepatoduodenal ligament may increase the difficulties and challenges during the laparoscopic approach [9]. Recently, several reports focused on how to overcome the current limitations of LH based on tumor location and underlying

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liver cirrhosis [10,11]. However, only a few reports discussed the condition of patients with a history of whole AS and then underwent LH. The importance and application of liver resection in this group of patients have gradually increased annually.

Therefore, the current study aimed to evaluate the difficulty and perioperative and postoperative outcomes of LH in patients diagnosed with primary HCC and with a history of nonhepatectomy AS.

MATERIALS AND METHODS

Patients and categorization

Data of patients with primary HCC undergoing LH at a tertiary referral center in eastern Taiwan from January 2013 to June 2021 were retrospectively collected. Patients diagnosed with recurrent HCC and synchronous malignancy were all excluded. A history of nonhepatectomy AS was defined as any operation entering the peritoneal cavity. Upper AS included previous abdominal surgeries with scars over the midline or paramedian incisions above the umbilicus and lower AS included surgeries with scars located below the umbilicus [12]. Transverse or oblique abdominal incisions were also classified as upper or lower AS based on their umbilical level. The history of cholecystectomy was highlighted from the upper AS as it would make more tissue reaction around the hepatoduodenal ligament and interfere with the Pringle maneuver preparation. Indocyanine green (ICG) 15-min retention rate was measured noninvasively on the day before liver resection. An ICG (25 mg) dissolved in saline (10 mL) was injected through a peripheral vein. The injected ICG dosage was 0.5 mg per kg of the patient. Patients were classified into the following two groups depending on the history of nonhepatectomy AS: patients with a history of nonhepatectomy (AS group, $n = 23$) and patients without a history of any AS (non-AS group, $n = 77$). The overall median follow-up duration was 29 months. The clinical data for these patients were retrospectively collected using medical records.

Terminology and definitions

The nomenclature from Brisbane 2000 Guidelines for liver anatomy and resection was used to describe the extent of hepatic resection [13]. Major resection was defined as resection of ≥ 3 segments, otherwise defined as minor resection. The IWATE criteria were used to evaluate the difficulty of laparoscopic liver resection [14]. The parenchymal transection time was defined as the duration of the Pringle maneuver plus the resting time during the Pringle maneuver, whereas the nonparenchymal transection time was defined as the total operation minus parenchymal transection time. The surgical video was also reviewed to calculate the parenchymal transection time for patients without the Pringle maneuver. The Clavien–Dindo classification was used to grade postoperative complications [15].

The definite diagnosis of diabetes mellitus (DM) was glycated hemoglobin level of $>6.5\%$ or under regular insulin control. Hypertension (HTN) was defined as systolic blood pressure of ≥ 140 mmHg or diastolic blood pressure of ≥ 90 mmHg or taking any antihypertensive medications.

Coronary artery disease (CAD) was defined as a history of CAD and undergoing treatment or even treatment based on CAD diagnosis.

Operative technique

First, a 12-mm trocar was inserted at the periumbilical area or virgin zone of the surgical scar in patients with a history of AS. After establishing pneumoperitoneum through the first insertion trocar, a 10-mm laparoscope was introduced, and then, additional 3–4 ports were made based on the adhesion condition and hepatectomy laterality. Adhesiolysis was performed by electrocautery, ultrasonic device (Harmonic scalpel[®], Ethicon, Cincinnati, OH, USA), or vessel sealing device (Ligasure, Medtronic, Minneapolis, MN, USA) when the surgical field would be compromised. After adhesiolysis, liver mobilization and hepatoduodenal ligament wrapping would be performed. Active and cycling Pringle maneuver was routinely performed to reduce blood loss and possible hepatocyte protection before bleeding during the parenchymal transection [16]. However, if the Pringle maneuver preparation would be interfered by severe adhesion around the hepatoduodenal ligament, the Pringle maneuver would not be adopted by the surgeon intraoperatively. Intraoperative sonography would be applied to identify and determine the tumor location, margin, and associated vascular distribution in the liver. Parenchymal transection was performed by electrocautery, ultrasonic device, or vessel sealing device under performing the Pringle maneuver. After completing the liver resection, meticulous hemostasis for the resection plane and the placement of a closed drainage tube was performed. The specimen was placed into the commercial tissue bag and extracted through the incision extension as per the surgeon's preference before wound closure. No hand-assisted technique was used in our series.

Statistical analysis

The Chi-square test was used to analyze for categorical variables, which were presented as numbers and percentages. Continuous variables were presented as medians with interquartile ranges and were analyzed with the Mann–Whitney U-test. The Kaplan–Meier curve with the log-rank test was used for the survival analysis. SPSS for MAC ver. 26 (SPSS Inc., Chicago, IL, USA) was used for the statistical analysis. $P < 0.05$ was considered statistically significant.

Ethic declaration

Ethical approval for this study (Research Ethics Committee, REC No. IRB 109-074-B) was provided by the Research Ethics Committee of Hualien Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation. Written informed consent was waived because the study was a retrospective data analysis.

RESULTS

The general characteristics of patients are indicated in Table 1, including 23 (23.0%) and 77 (77.0%) patients in the AS and non-AS groups, respectively. Male patients were dominant, and comorbidity rates, including DM, HTN, and CAD were not significantly different in both the groups. The mean age of patients was similar in both the groups (67 vs. 66 in the AS and non-AS groups, respectively; $P = 0.684$).

Table 1: Patient characteristics

Characteristics	Whole cohort (n=100)	AS group (n=23)	Non-AS group (n=77)	P
Age*	66±9	67±10	66±9	0.684
Gender, male (%)	80.0 (80/100)	78.3 (18/23)	80.5 (62/77)	0.812
BMI (kg/m ²) [§]	25.6 (23.1-28.8)	25.5 (22.7-28.0)	25.6 (23.2-29.5)	0.258
Comorbidity (%)				
DM	44.0 (44/100)	34.8 (8/23)	46.8 (36/77)	0.347
HTN	55.0 (55/100)	43.5 (10/23)	58.4 (45/77)	0.238
CAD	8.0 (8/100)	8.7 (2/23)	7.8 (6/77)	0.889
FEV1 (%)*	89.1±19.7	87.0±24.7	89.6±18.4	0.135
FEV1/FVC (%)*	77.0±9.7	69.7±13.7	78.8±7.6	0.020
LVEF (%)*	74.3±9.0	76.6±9.2	73.5±8.8	0.816
Child-Pugh classification Stage A (%)	99.0 (96/97)	100.0 (21/21)	98.7 (75/76)	0.597
MELD-Na score [§]	8 (7-10)	7 (7-8)	8 (7-10)	0.010
ALBI grade				
Grade I	61.9 (60/97)	76.2 (16/21)	57.9 (44/76)	0.295
Grade II	37.1 (36/97)	23.8 (5/21)	40.8 (31/76)	
Grade III	1.0 (1/97)	0.0 (0/21)	1.3 (1/76)	
ICG-15 (%) [§]	10.5 (5.1-16.6)	9.3 (4.0-17.2)	11.0 (6-17)	0.600
Viral hepatitis status (%)				
HBV	53.0 (53/100)	65.2 (15/23)	49.4 (38/77)	0.538
HCV	21.0 (21/100)	13.0 (3/23)	23.4 (18/77)	
Non-B, Non-C	13.0 (13/100)	13.0 (3/23)	13.0 (10/77)	
HBV pulse HCV	13.0 (13/100)	8.7 (2/23)	14.3 (11/77)	

*Normal distribution, [§]Nonnormal distribution, AS: Abdominal surgery group, DM: Diabetes mellitus, HTN: Hypertension, CAD: Coronary artery disease, FEV1: Forced expiratory volume in 1 s, FVC: Forced vital capacity, LVEF: Left ventricular ejection fraction, MELD-Na: Model for end-stage liver disease-Na, ALBI grade: Albumin-bilirubin grade, ICG: Indocyanine green, BMI: Body mass index, HBV: Hepatitis B virus, HCV: Hepatitis C virus

The preoperative cardiopulmonary function tests showed that the mean left ventricular ejection fraction was similar in the AS and non-AS groups (76.6% vs. 73.5%, $P = 0.816$), and the mean ratio of forced expiratory volume in 1 s to forced vital capacity was worse in the AS group (69.7% vs. 78.8%, $P = 0.020$). The majority of patients in both the groups were classified Child-Pugh class A. The median MELD-Na score (7 vs. 8, $P = 0.321$), albumin-bilirubin grade ($P = 0.295$), and preoperative ICG 15-min retention rate (9.3% vs. 11.0%, $P = 0.600$) were not significantly different in the AS and non-AS groups. The viral hepatitis status of both the groups was also similar with 53.0% HBV, 21.0% HCV, 13.0% HBV/HCV, and 13.0% non-HBV/HCV. The distribution of previous abdominal surgeries is listed in Table 2. The majority of patients (43.5% in both the groups) underwent previous upper and lower abdominal surgeries.

No differences were observed in the distribution of major hepatectomy between the two groups [Table 3]. The median IWATE difficulty score for LH was 5 (3–7) and 5 (3–8) in the AS and non-AS groups, respectively ($P = 0.194$). No significant difference was also observed in the median operative time (219 vs. 200 min, $P = 0.609$), median intraoperative blood loss (100.0 vs. 200.0 mL, $P = 0.734$), intraoperative transfusion rate (4.3% vs. 10.4%, $P = 0.374$), median duration of parenchymal transection (90.0 vs. 72.4 min, $P = 0.673$), and median duration of nonparenchymal transection (191.0 vs. 125.0 min, $P = 0.228$) between the AS and non-AS groups. The conversion rate was 3.9% ($n = 3$) in the non-AS group (one experienced uncontrollable bleeding from inferior hepatic vein with unstable hemodynamic status during parenchyma transection; the second one experienced

difficulty in approach to inferior vena cava zone with massive bleeding during parenchyma transection; the third one experienced lymphadenopathy at hilar region and group eight region with suspicious cholangiocarcinoma and converted to laparotomy for further lymph nodes dissection before performing parenchyma transection) and none of the patients in the AS group were converted to laparotomy ($P = 0.336$). The pathology report showed no significant difference of the median tumor size (2.5 vs. 3.0 cm; $P = 0.167$) and the marginal status (0.3 vs. 0.5 cm; $P = 0.217$) in the AS and non-AS groups. Most of the tumor was grade II (58.0%). No significant was noted over the ratio of angiolymphatic invasion (52.2% vs. 55.8%, in the AS group and in non-AS group, respectively; $P = 0.814$). The surgical complication rate did not differ in both the groups (30.3% vs. 33.8% in the AS and non-AS groups, respectively; $P = 0.488$) mainly in grades 1 and 2, and no 30-day mortality occurred in this series. The postoperative hospital stay was nearly identical in both the groups. No significant difference was observed in the 2-year and overall survival (82.4% vs. 85.9%; $P = 0.820$) and disease-free survival (65.8% vs. 56.8%; $P = 0.155$) between AS and non-AS groups [Figures 1 and 2].

DISCUSSION

The incidence of peritoneal adhesions is 70%–95% after laparotomy, although 10%–25% of the general population may have peritoneal adhesions even without previous surgery [17–20]. In laparoscopic surgeries, there is an increased risk of conversion to laparotomy, intraoperative complications, and longer operative time [21]. Therefore, a history of AS has been considered a relative contraindication for laparoscopic

surgery during the early years of this kind of procedure. However, as the skills, instruments, and video systems of laparoscopy gradually improved annually, laparoscopic interventions, such as cholecystectomy, colectomy, and even gastrectomy, have been safely used in patients with a history of AS [22-25]. As LH is still a technically demanding procedure, only a few reports have demonstrated laparoscopic liver resection performed on patients with a history of abdominal surgical intervention. Therefore, this study focused on analyzing the cohort of patients who underwent LH for primary HCC with a history of nonhepatectomy abdominal surgical intervention.

The LH procedure is performed in the following steps: trocar insertion, possible adhesiolysis, liver mobilization, performing intraoperative sonography for lesion localization, Pringle maneuver preparation, parenchyma transection, and hemostasis. Several studies had already reported that a history of AS would prolong the LH total operative time, including all of the abovementioned procedures within 15–91 min [9,12,26-29].

Table 2: Types of previous abdominal surgeries

Type	n (%)
Upper abdominal surgery	10 (43.5)
Cholecystectomy	3 (13)
Lower abdominal surgery	10 (43.5)

Table 3: Perioperative results, pathology findings, and postoperative results

Characteristics	Whole cohort (n=100)	AS group (n=23)	Non-AS group (n=77)	P
Major resection (%)*	14.0 (14/100)	4.3 (1/23)	16.9 (13/77)	0.128
IWATE score [§]	5 (3-8)	5 (3-7)	5 (3-8)	0.194
Operative time (min) [§]	204 (157-274)	219 (156-344)	200 (158-267)	0.609
Pringle maneuver (%)	70.0 (70/100)	39.1 (9/23)	79.2 (61/77)	0.001
Pringle duration (min) [§]	55.5 (32.2-85.8)	69.2 (41.0-101.5)	55.0 (31.0-85.0)	0.424
Parenchymal transection time (min) [§]	80.0 (45.0-122.2)	90.0 (50.0-136.5)	72.4 (43.7-118.6)	0.673
Nonparenchymal transection time (min) [§]	129.0 (87.0-185.0)	191.0 (75.6-322.8)	125.0 (90.1-174.5)	0.228
Blood loss (mL) [§]	200.0 (50.0-500.0)	100.0 (50.0-900.0)	200.0 (50.0-425.0)	0.734
Conversion (%)	3.0 (3/100)	0.0 (0/23)	3.9 (3/77)	0.336
Intraoperative transfusion (%)	9.0 (9/100)	4.3 (1/23)	10.4 (8/77)	0.374
Drainage tube placement (%)	78.0 (78/100)	78.3 (18/23)	77.9 (60/77)	1.000
Solitary tumor (%)	86.0 (86/100)	82.6 (19/23)	87.0 (67/77)	0.593
Size (cm) [§]	3.0 (2.2-4.1)	2.5 (1.5-4.0)	3.0 (2.4-4.3)	0.167
Margin (cm) [§]	0.5 (0.2-1.2)	0.3 (0.1-0.9)	0.5 (0.2-1.4)	0.217
Histology grading (%)				
Grade I	8.0 (8/100)	13.1 (3/23)	6.5 (5/77)	0.107
Grade II	58.0 (58/100)	39.1 (9/23)	63.6 (49/77)	
Grade III	34.0 (34/100)	47.8 (11/23)	29.9 (23/77)	
Angiolymphatic invasion (%)	55.0 (55/100)	52.2 (12/23)	55.8 (43/77)	0.814
Ishak score [§]	4 (2-5)	3 (2-4)	4 (2-6)	0.055
Complications (%)				
1+2	30.0 (30/100)	26.0 (6/23)	31.2 (24/77)	0.488
3a	1.0 (1/100)	0.0 (0/23)	1.3 (1/77)	
3b	0.0 (0/100)	0.0 (0/23)	0.0 (0/77)	
4a	1.0 (1/100)	4.3 (1/23)	0.0 (0/77)	
4b	1.0 (1/100)	0.0 (0/23)	1.3 (1/77)	
B	0.0 (0/100)	0.0 (0/23)	0.0 (0/77)	
Time to remove drainage tube (days) [§]	6 (4-7)	5 (4-6)	6 (5-7)	0.142
Postoperative hospital stay (days) [§]	7 (5-8)	6 (5-7)	7 (6-8)	0.060

*Normal distribution, [§]Nonnormal distribution. AS: Abdominal surgery group

Overall, the duration for trocar insertion, liver mobilization, performing intraoperative sonography for lesion localization, and the Pringle maneuver preparation did not significantly vary in each operation. However, the varied operative time would be caused by difficulty in performing adhesiolysis, tumor location, and size of the transection plan. Consequently, prolonged operative time cannot be only attributed to adhesion caused by previous AS.

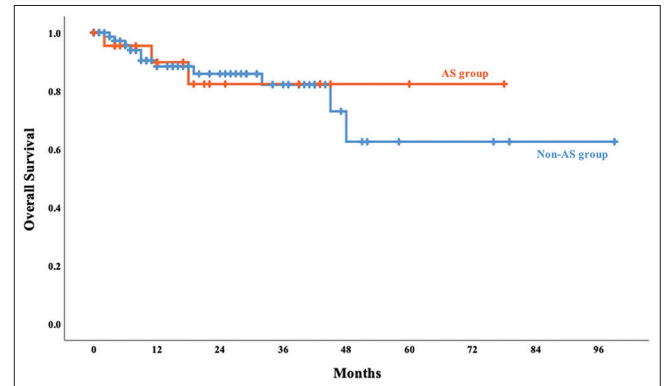


Figure 1: The Kaplan–Meier curve of overall survival in the AS and non-AS groups. The 12-and 24-month overall survival rates were 89.8% and 82.4% in the AS group and 88.4% and 85.9% in the non-AS group. Log-rank test, *P* = 0.820. AS: Abdominal surgery, non-AS: Nonabdominal surgery

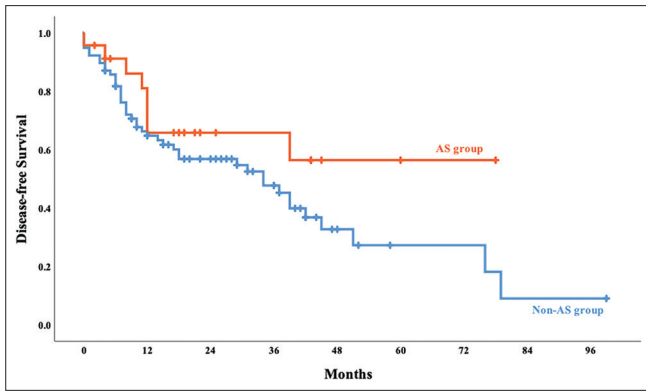


Figure 2: The Kaplan–Meier curve of disease-free survival in the AS and non-AS groups. The 12- and 24-month disease-free survival rates were 81.0% and 65.8% in the AS group and 64.8% and 56.8% in the non-AS group. Log-rank test, $P=0.155$. AS: Abdominal surgery, non-AS: Nonabdominal surgery

Unlike previous studies that only determined the overall operative time, this is the first study that divided the operative time into parenchymal and nonparenchymal transection phases. The total operative time was divided into two phases to identify the duration and complexity of adhesiolysis during the nonparenchymal transection phase, which may indicate the difficulty caused by previous nonhepatectomy surgery and specifically attribute the difficulty of tumor resection to parenchymal transection phase. Besides, we also calculated the IWATE difficult score to identify the difficulty of tumor resection. Under this condition, a previous AS led to longer nonparenchymal transection time of up to 66 min specifically for the adhesiolysis procedure. Conversely, the duration of parenchymal transection and the mean IWATE difficulty score were not significantly different in patients who underwent AS or not. In addition, based on learning from extensive experiences of adhesiolysis using the laparoscopic intraperitoneal onlay mesh technique in our daily practice, no adhesiolysis-related conversion occurred in the AS group although prolonged nonparenchymal transection time, with the conversion rate of approximately 4.5%–14.3% mainly caused adhesion according to previous reports [9,12,28].

With regard to other parameters, such as blood loss, transfusion rate, and postoperative hospital stay, previous surgery was not interfered by but was compatible with several previous studies [9,12,27,30–33]. When comparing complications reported in a previous study, i.e., 13.2%–31.0% and 13.5%–17.0% in AS and non-AS groups [9,12,28], major complications (above grade 3) were 4.3% and 2.6% in the AS and non-AS groups, respectively, without mortality in our series. With the adequate and delicate adhesiolysis during the operation, it will not increase the difficulty in parenchyma transection. It will not increase the short-term complication and will not compromise the long-term survival.

This study has some limitations. First, this retrospective and nonrandomized review had a relatively small sample size. Second, the specific grading system for adhesion severity was not used in this study. Third, the effects of the interval between previous nonhepatectomy AS and LH index cannot be investigated. Fourth, most of the patients in AS group received

minor resection, though not achieved significant, but was not similar to the ratio of minor resection of non-AS group.

CONCLUSIONS

A history of nonhepatectomy abdominal operation leads to a longer nonparenchymal transection time of approximately 66 min. Prolonged nonparenchymal transection time indicated more delicate and complicated adhesiolysis and did not indicate the LH difficulty and also did not cause adhesion-related conversion. Surgical complications, postoperative hospital stay, and survival outcomes were not compromised. LH did not increase the difficulty in patients with previous nonhepatectomy AS without causing a conversion.

Data availability statement

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Nil.

Conflicts of interest

Dr. Ming-Che Lee, an editorial board member at *Tzu Chi Medical Journal*, had no role in the peer review process of or decision to publish this article. The other authors declared no conflicts of interest in writing this paper.

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