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Liver hanging maneuver is suitable in major hepatectomy for liver malignancies over 5 cm

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ABSTRACT

Objective: Hepatic transection through an anterior approach is required to successfully complete anatomical hepatectomy for large liver malignancies. The liver hanging maneuver (LHM) is an alternative procedure for transection on an adequate cut plane and may reduce intraoperative bleeding and transection times.

Material and Methods: We examined the medical records of 24 patients with large liver malignancies (>5 cm) who had undergone anatomical hepatic resection with LHM (n= 9) or without LHM (n= 15) between 2015 and 2020. Patient demographics, preoperative hepatic function, surgical records, and post-hepatectomy outcomes were retrospectively compared between the LHM and non-LHM groups.

Results: The prevalence of tumors >10 cm was significantly higher in the LHM group than in the non-LHM group ($p< 0.05$). Furthermore, LHM was significantly performed to right and extended right hepatectomies in the background normal liver ($p< 0.05$). Although transection times did not significantly differ between the two groups, the amount of intraoperative blood loss was slightly lower in the LHM group than in the non-LHM group (1.566 mL vs. 2.017 mL), and blood transfusion was not needed for patients in the LHM group. Post-hepatectomy liver failure and bile leakage were not observed in LHM. However, the length of hospitalization was slightly shorter in the LHM group than in the non-LHM group.

Conclusion: LHM is useful for transecting an adequately cut plane in hepatectomy for liver tumors over 5 cm-in-size located on the right side and achieves better outcomes.

Keywords: Large intrahepatic malignancies, anterior hepatectomy, liver hanging maneuver, blood loss

INTRODUCTION

In major hepatectomy, reducing intraoperative blood loss and the need for transfusions may minimize postoperative tumor relapse and prolong the survival of patients with primary liver cancer (1,2). In cases in which large liver tumors occupy and compress the main intrahepatic vasculature, transection of the liver parenchyma through an anterior approach without mobilization of the remnant liver is preferable because the avoidance of liver rotation has the advantages of circumventing tumor dissemination and/or injury produced by compression of the remnant liver (3). Furthermore, a longer transection time due to the loss of the transection plane may increase blood loss.

Belghiti et al. (4) have proposed the liver hanging maneuver (LHM) for right hepatectomy without liver mobilization using a nasogastric tube inserted into the free space between the avascular vena cava surface and the backside of the caudate liver. The lifting of this tube or tape allows parenchymal transection in a deeper site and transection that avoids short hepatic veins (5). LHM has been attracting increasing interest worldwide for major anatomical hepatectomy, particularly that for large liver tumors or tumors compressing the surrounding vascular architecture (6-8). This technique has recently been applied for less invasive anatomical resection (9). Moreover, the transected and remnant liver are both rotated to the counter side by lifting the hepatic back side during transection (8), which is useful for successfully transecting the deeper parenchyma in the final step. Although the primary author had already published a pilot study article on LHM over 10 cm at another institute in the 2000s, in comparisons with the conventional rotated procedure, it currently remains unclear whether LHM minimizes blood loss or reduces transection

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times. Since various transection procedures and materials have recently been developed, LHM alone is not as useful in most cases (10,11). At the time of recent stable time since the 2010s in comparison with a decade ago, further studies are warranted to clarify the significance of LHM in the current era.

To clarify our hypothesis on the minimization of blood loss and reductions in transection times, we retrospectively and historically examined surgical data on liver malignancies large over 5 cm in patients who underwent major hepatectomy and compared these parameters with those of patients who underwent liver resection with or without LHM at a different academic institute.

MATERIAL and METHODS

Study Design and Patients

The study protocol for database access and review, ethics and non-conflict of interests were approved by the Institutional Medical Board of University of Miyazaki Hospital between April 2015 and December 2020 (reference number O-0898, on February 18th, 2021). Patient consent was obtained by the opt-out procedure for one month on the hospital's website in march, but with no disclaimer. We performed liver resection (including more than three segmentectomies) on 24 patients with liver malignancies >5 cm; nine patients (38%) underwent LHM (the LHM group) according to the policy of the first author while the remaining 15 patients underwent resection without LHM (the non-LHM group) by another experienced surgeon's choice and were compared as the control.

Clinical and Surgical Parameters

The following data were collected for analysis: age, sex, background liver disease, liver disease, preoperative liver functions (indocyanine green retention rate at 15 minutes), liver uptake ratio by technetium-^{99}m-galactosyl, human serum albumin, liver scintigraphy, surgical procedure or records (extent of hepatectomy, surgical device, vena cava clamping, operation time, time for liver parenchymal transection, blood loss, and blood transfusion), post-hepatectomy-related complications (uncontrolled ascites, intraabdominal abscess, bile leakage, and hepatic failure), and duration of hospitalization. Uncontrolled ascites or pleural effusion was defined by the use of diuretics for more than two weeks.

The surgical procedure included J-shaped incision laparotomy (upper median plus right-sided transverse incision to the ninth intercostal space) (11). The falciform ligament was cut to expose the confluences of the right, middle, and left hepatic veins and the anterior surface of the vena cava. Mobilization of the remnant liver was not performed on patients who underwent LHM. LHM was conducted according to the method described by Belghiti et al (4). The space between the right and middle hepatic veins was dissected using a right-angled clamp. Loose connective tissue between the anterior surface of the vena cava and the paracaval caudate lobe was dissected from this space using a long Kelly clamp at the space without short hepatic veins (12). A 10-Fr nasogastric tube was inserted and passed easily through the dissecting space. We completed tube insertion within approximately 10 minutes. The tube was then lifted up for LHM. The cut plane along the middle or umbilical fissure hepatic vein was hung up by the tube as previously reported (8). Various anatomical resections are possible using the tube re-positioning technique, as described by Kokudo et al. (13). Hemostatic devices, such as LigaSure®, and ultrasonic coagulation instruments were consistently used in the present series. Hepatic transection was mainly performed in combination with the crush clamping method, while an ultrasonic dissector was used for dissection around the main vessels at the hepatic hilum or inferior vena cava (IVC) (14). Hepatic inflow was intermittently occluded during transection using the Pringle maneuver (15 minutes of occlusion and five minutes of de-clamping) (15). In cases in which bleeding from the compressed hepatic vein was not controlled during hepatectomy, the infrahepatic vena cava was taped and semi-clamping was performed by maintaining central venous pressure (16,17).

Statistical Analysis

The primary endpoints were blood loss and transection times under Pringle's maneuver during hepatectomy, and secondary endpoints were post-hepatectomy morbidity and mortality and length of hospitalization. Continuous data were expressed as means ± SD. Data for different groups were compared using a one-way analysis of variance (ANOVA). Chi-squared test was used for comparisons of categorical variables. Differences between the groups were analyzed by Fisher's exact test or Scheffé's multiple comparison test. A two-tailed p-value of less than 0.05 was considered to be significant. Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS) software, version 22.0 (IBM, Chicago, IL, USA).

RESULTS

Table 1 summarizes demographic and surgical data and comparisons of the LHM and non-LHM hemihepatectomy groups. No significant differences were observed in age or sex between the two groups. Comparisons of background liver diseases and liver tumors showed no significant differences between the non-LHM and LHM groups. Furthermore, the results of preoperative liver function tests did not significantly differ between the two groups. However, the prevalence of tumors >10 cm was significantly higher in the LHM group than in the non-LHM group ($p < 0.05$).

Operative procedure, thoracotomy, extent of hepatectomy, and use of vena cava clamping and surgical devices did not significantly differ between the two groups. Furthermore, no significant differences were observed in the transection time (similar

Table 1. Comparison of patient demographics, surgical records, and postoperative outcomes

	LHM group, n= 9	Non-LHM group, n= 15	p
Age	65 ± 12	62 ± 21	0.907
Sex (male/female)	9 (100)/0	12 (80)/3 (20)	0.225
Background liver			
Normal/chronic hepatitis/cirrhosis/NAFLD/CASH/ jaundice	1 (11)/2 (22)/0/2 (22)/3 (34)/1 (11)	7(47)/2 (13)/2 (13)/1 (7)/1 (7)/2 (13)	0.295
Diseases			
HCC/CCC/CLM/others	4 (44)/1 (11)/2 (22)/1 (11)	6 (40)/3 (20)/6 (40)/0	0.485
Tumor size			
5-10 cm/>10 cm	2 (22)/7 (78)	10 (67)/5 (33)	**0.049**
Preoperative liver functions			
Liver damage grade A/B*	9 (100)/0	15 (100)/0	1.0
Indocyanine green retention rate at 15 minutes (%)	13.1 ± 4.7	9.7 ± 5.4	0.069
Preoperative hyaluronic acid level (ng/mL)	68 ± 44	90 ± 55	0.492
Liver uptake ratio by GSA liver scintigraphy	0.93 ± 0.03	0.94 ± 0.02	0.702
Surgical records			
Thoracotomy (No/Yes)	7 (78)/2 (22)	9 (60)/6 (40)	0.455
Liver stiffness (Soft/Hard)	9 (100)/0	11 (73)/4 (27)	0.259
Blood loss (mL)	1566 ± 1243	2117 ± 1934	0.558
Red cell transfusion (No/Yes)	3 (34)/6 (66) (938 mL)#	6 (40)/9 (60) (1.056 mL)	0.999
Total operation time (minutes)	488 ± 152	544 ± 139	0.385
Transection time under inflow occlusion (minutes)	56.4 ± 13.5	68.1 ± 64.4	0.999
Procedures			
(hemi-/extended hemi-/trisectionectomy)	5 (56)/3 (33)/1 (11)	11 (73)/3 (20)/1 (7)	0.205
Right-side/Left-side hepatectomy	8 (89)/1 (11)	7 (47)/8 (53)	**0.018**
Postoperative liver function			
Maximum total bilirubin (mg/dL)	0.68 ± 0.20	0.83 ± 0.46	0.744
Maximum ALT (IU/L)	425 ± 444	547 ± 345	0.209
Minimum prothrombin activity (%)	54 ± 10	49 ± 14	0.503
Patient outcome			
Morbidity (No/Yes)	8 (89)/1 (11)	14 (93)/1 (7)	0.999
Hepatic failure (No/Yes)	9 (100)/0	13 (87)/2 (13)	0.551
Uncontrolled ascites (No/Yes)	7 (78)/2 (22)	12 (80)/3 (20)	0.999
Bile leakage (No/Yes)	9 (100)/0	12 (80)/3 (20)	0.999
Hospital stay (days)	24.2 ± 10.4	30.0 ± 8.9	0.135

Parenthesis shows the ratios (percentage).
Liver Damage grade guided by the General Rules for the Clinical and Pathological Study of Primary Liver Cancer in Japan (16).
GSA: Galactosyl serum albumin, NAFLD: Non-alcoholic fatty liver disease, CASH: Chemotherapy-associated fatty liver disease in colorectal cancer patients, HCC: Hepatocellular carcinoma, CCC: Cholangiocellular carcinoma, CLM: Colorectal liver metastasis, GSA: Galactosyl serum albumin, ALT: Alanine transaminase.
#Mean value in patients who received blood transfusions.

to the time of the clamping of hepatic blood inflow), amount of intraoperative blood loss, blood transfusion, or total operation time between the two groups. However, the prevalence of right hepatectomy was significantly higher in the LHM group than in the non-LHM group ($p< 0.05$).

Results on postoperative complications and outcomes were compared. Regarding postoperative complications, no significant differences were observed in the total complication rate between the non-LHM and LHM groups. Furthermore, the prevalence of hepatectomy-related complications and the length of hospitalization did not significantly differ between the two groups. No in-hospital deaths were recorded in the present study.

DISCUSSION

We previously reported another population, limited to large hepatocellular carcinoma (HCC) (>10 cm), between 2000 and 2007, which included initial hepatectomy during a technical learning curve for the first author at a different institute as a pilot study (18). The findings obtained showed significantly less intraoperative blood loss (1.269 ± 1.407 mL) and shorter transection times (39.7 ± 10.5 minutes) than those by another operator (19). In patients with a large tumor or tumor that invaded adjacent organs, anterior liver transection was preferably performed through the LHM procedure, and hepatic vein transection or the combined resection of invasive parts was conducted in the final step after complete transection to the front of the vena cava. In 2003, Kokudo et al. (13) proposed the gradual tape-repositioning technique for cases of living liver donation, in which the tape is inserted by passing it between Glisson's pedicle and the liver parenchyma. When such reports were published on LHM, LHM had already been performed for various types of anatomical hepatectomies (6,7,20). However, Shindoh et al. reported that LHM for HCC was rarely performed in hepatectomy in a larger series, this procedure did not appear to be the standard, and a conventional anterior approach without LHM was applied in laparoscopic right hepatectomy developed after the 2010s (10). Since the first author performed LHM or hepatectomy when he moved to the present institute, reconfirming the significance of LHM for large liver tumors was attempted in the present study because other experienced operators routinely performed conventionally mobilized hepatectomy without LHM, even for large tumors at this institute.

We compared clinical parameters and outcomes of a small number of patients between the LHM and non-LHM groups in a non-random manner, which is a limitation of the present study. As shown in Table 1, the background and preoperative liver functional reserve in patients in both groups did not significantly differ; however, liver tumors >10 cm were more likely to be treated by the first author and LHM was preferably applied for cases in which mobilization of the resected liver was difficult. However, although tumor characteristics, type of surgical intervention and surgical teams were compared in the two groups, tumor diameter exceeding 10 cm and right hepatectomy rates were significantly higher in the LHM group. Thus, the small number of patients and the retrospective nature of the study reduce the power of the study and make it difficult to interpret precisely. In the next step, a prospective study must be planned by setting these background. Surgical records showed that LHM did not reduce blood loss or transection times from those in the non-LHM group, and this may have been influenced by the selection bias of liver tumors as described above. Furthermore, the present results on blood loss (1566 ± 1243 mL) and transection times (56.4 ± 13.5 minutes) were consistent with previous findings (18). The lead author did not improve the procedures of LHM although the subjects were different between the previous and present LHM studies. Autologous blood transfusion was performed for most cases in the present series, whereas those in the previous series received allogenic transfusion. Blood transfusion, which affects the prognosis of cancer patients, does not appear to be involved in the present case (21).

The application of LHM in right hemi-hepatectomy was significantly more frequent in this cohort. In the case of left hepatectomy, LHM did not appear to be useful because the conventional technique was generally not difficult in many cases. In the LHM group, left-side hepatectomy was trisectionectomy because the operative field around the retrohepatic space was not clearly visualized due to the volume of the liver. Postoperative liver function and patient outcomes were similar and no mortalities occurred, which was consistent with our previous findings (18). In summary, potential reasons for the application of LHM include:

1) Dissection of the liver parenchyma along the main intrahepatic vasculature, particularly hepatic veins compressed by a large liver tumor;

2) Transection in a deeper part near the vena cava may be rapidly performed without injury to the vena cava or short hepatic veins due to shielding with covering tape;

3) Confirming the root of hepatic veins in the case of right hepatectomy and right or left trisectionectomy accompanied identification of the roots of the hepatic veins in right hepatectomy and left or right trisectionectomy in patients with a larger liver volume.

Since half-clamping of the infrahepatic vena cava (16,17) may prevent bleeding from hepatic veins because of a decrease in central venous pressure, we sometimes applied this procedure. However, surgical records did not significantly differ between the present and previous studies (18). According to the vascular anatomy or physique of patients, the application of IVC clamping is needed for large liver tumors compressing the IVC or hepatic veins (17). Regarding parenchymal transection, transecting or hemostatic devices were useful for reducing transection times (14); however, their utility for the control of hepatic venous bleeding remains unclear. Therefore, the development of novel hemostatic compound substances during transection is required (22); however, the use of fibrin glue did not appear to control parenchymal bleeding in hepatectomy (23). This study compares the results of two surgeons who did and did not perform LHM and the two groups were not similar in terms of the removed liver side and tumor sizes. Due to these disadvantages, the two groups might not be able to be precisely compared with each other. Although there is no statistical difference in comparisons, it is suggested that some parameters are advantageous over the other one. Under the light of these results, it seemed that there is no significantly difference between the two groups.

We previously reported that limited liver mobilization LHM may prevent prolonged ascites by limiting the detachment of ligament tissue around the liver (4,20). However, in the present study, ascites was controlled well, and this result was attributed to the use of novel diuretics as vasopressin receptor inhibitors (Tolvaptan, Otsuka Pharmaceutical Co., Tokyo, Japan). Recent advances in not only surgical techniques, but also perioperative management have also improved patient outcomes.

CONCLUSION

We herein examined the suitability of LHM in major hepatectomy for large liver malignancies using a retrospective cohort study at a single academic institute. The use of LHM was useful in right hepatectomy or trisectionectomy for large liver tumors because it may be useful in identifying the target site of parenchymal resection and an adequate transected plane along compressed hepatic veins for large malignancies.

Ethics Committee Approval: The study protocol was approved by the Institutional Review Board of University of Miyazaki (Decision no: C-0898, Date: 18.02.2021). Written and informed consent was obtained from the opt-out method on our website. All study protocols followed guidelines stated in the Declaration of Helsinki.

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Conflict of Interest: The authors have no conflicts of interest to declare.

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Karaciğer asma manevrası, 5 cm üzerindeki karaciğerin malign tümörlerinde majör hepatektomi için uygundur: Retrospektif kohort çalışması

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ÖZET

Giriş ve Amaç: Karaciğerin büyük malign tümörlerinde anatomik hepatektomiyi başarıyla tamamlamak için önden yaklaşımla hepatik transeksiyon gereklidir. Karaciğer asma manevrası [*liver hanging maneuver* (LHM)] yeterli bir kesme düzleminde transeksiyon için alternatif bir prosedürdür ve intraoperatif kanama ve transeksiyon sürelerini azaltabilir.

Gereç ve Yöntem: 2015-2020 yılları arasında LHM (n= 9) ile veya LHM (n= 15) olmadan anatomik hepatik rezeksiyon yapılan ve karaciğerin büyük malign tümörleri (>5 cm) olan 24 hastanın tıbbi kayıtlarını inceledik. Hasta demografisi, preoperatif hepatik fonksiyon, cerrahi kayıtlar ve post-hepatektomi sonuçları LHM ve LHM dışı gruplar arasında retrospektif olarak karşılaştırıldı.

Bulgular: LHM grubunda 10 cm> tümör prevalansı LHM olmayan gruba göre anlamlı olarak daha yüksekti (s< 0,05). Ayrıca, LHM arka plan normal karaciğerinde sağ ve genişletilmiş sağ hepatektomilere anlamlı olarak daha sık yapıldı (s< 0,05). Transeksiyon süreleri iki grup arasında anlamlı olarak farklılık göstermese de LHM grubunda intraoperatif kan kaybı miktarı LHM dışı gruba göre daha düşüktü (1,566 mL ile 2,017 mL) ve LHM grubundaki hastalar için kan nakline gerek duyulmadı. LHM'de hepatektomi sonrası karaciğer yetersizliği ve safra kaçağı gözlenmedi. Ancak LHM grubunda hastaneye yatış süresi LHM olmayan gruba göre biraz daha kısaydı.

Sonuç: LHM, sağ tarafta bulunan büyük karaciğer tümörleri için uygulanan hepatektomide transeksiyon planını uygun şekilde bölmek için yararlıdır ve daha iyi sonuçlar elde edilmektedir.

Anahtar Kelimeler: Büyük intrahepatik maligniteler, anterior hepatektomi, karaciğer asma manevrası, kan kaybı

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