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Clinical Report

Feasibility of Precoagulation Without the Pringle Maneuver for Endoscopic Hepatectomy of Cirrhotic Liver

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Abstract: Various methods, devices, and techniques have been developed to improve safety during laparoscopic hepatectomy procedures. Among these, the Pringle maneuver (PM) is widely used to minimize blood loss during liver transections; however, the risk of ischemic injury associated with this technique is increased by poor hepatic reserve and regeneration dysfunction secondary to liver cirrhosis. This retrospective study evaluated the short-term outcomes and feasibility of precoagulation for endoscopic hepatectomy without PM in patients with liver cirrhosis. Eleven patients with liver cirrhosis who also underwent endoscopic hepatectomy for hepatocellular carcinoma were recruited to undergo either microwave tissue coagulation or radiofrequency ablation for precoagulation before liver transection. A wedge resection without the PM was performed in all patients, with seven patients selected for bipolar radiofrequency ablation and four patients for microwave coagulation therapy. The procedures included video-assisted thoracoscopic hepatectomy in two patients and laparoscopic hepatectomy in nine patients. One patient who underwent radiofrequency ablation developed postoperative bleeding (Clavien-Dindo grade Ⅲ). In conclusion, precoagulation can help to minimize intraoperative blood loss without the PM, contributing to effective resection of liver tumors. We propose that precoagulation could serve as a standard technique for endoscopic hepatectomy in patients with cirrhosis.

Key words: laparoscopic hepatectomy, thoracoscopic hepatectomy, precoagulation, liver cirrhosis, Pringle maneuver

Introduction

Blood loss during hepatectomy necessitating perioperative blood transfusion has a direct negative effect on the postoperative course and oncological outcome of patients[1,2]. Multiple reports support the feasibility, safety, and benefits of laparoscopic over open hepatectomy[3-10]. Furthermore, laparoscopic hepatectomy (LH) was recently suggested as feasible even in patients

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with cirrhosis[3, 9]; however, transection of cirrhotic liver parenchyma is technically difficult, and increased bleeding can occur secondary to fibrosis, portal hypertension, and coagulopathy. Consequently, a standard method of LH in patients with cirrhosis has not been established.

The Pringle maneuver (PM) is widely used to minimize blood loss during liver transection. Liver ischemia-reperfusion, wherein many inflammatory cytokines are produced due to an increased warm ischemia time, can induce injury in liver cells and hepatic sinusoidal endothelial cells[11], and cirrhotic liver tissue is especially susceptible to ischemia-reperfusion injury[12]. Therefore, if it is possible to safely transect cirrhotic liver parenchyma with poor hepatic reserve and regeneration dysfunction, the PM should be avoided if possible to prevent ischemia-reperfusion injury.

Radiofrequency ablation (RFA)-assisted hepatectomy was first reported in 2002[13], and precoagulation using such techniques could reduce intraoperative blood loss, lower transfusion rates, and decrease the risk of postoperative morbidity and mortality[14–16]. Precoagulation is thus recommended for patients with liver cirrhosis[17, 18].

In this study, we investigated the feasibility of precoagulation for patients with liver cirrhosis undergoing endoscopic hepatectomy (EH) not involving the PM.

Patients and methods

Patients

From January 2000 to December 2017, 150 patients underwent LH or thoracoscopic hepatectomy (TH) at Showa University Hospital. Of these, 11 patients who underwent EH for hepatocellular carcinoma with cirrhosis were recruited for this retrospective study. The selected cases were diagnosed as stage F4 liver cirrhosis based on pathological findings. Table 1 lists the patient characteristics.

Table 1. Characteristics of patients who underwent endoscopic hepatectomy for hepatocellular carcinoma

Variable	n = 11
Age in years, median (range)	61 (59–76)
Male/female, n	8/3
Body mass index, mean (range)	23.1 (18.1–29.5)
Comorbidities, n	
Cardiovascular disease	3
Diabetes	4
Pulmonary disease	1
Child-Pugh score of A/B, n	7/4
Preoperative laboratory data, mean (range)	
Total bilirubin (mg/dl)	1.07 (0.6–1.5)
Aspartate transaminase (U/l)	48 (21–98)
Alanine transaminase (U/l)	43 (17–93)
Prothrombin time (%)	75 (57–100)

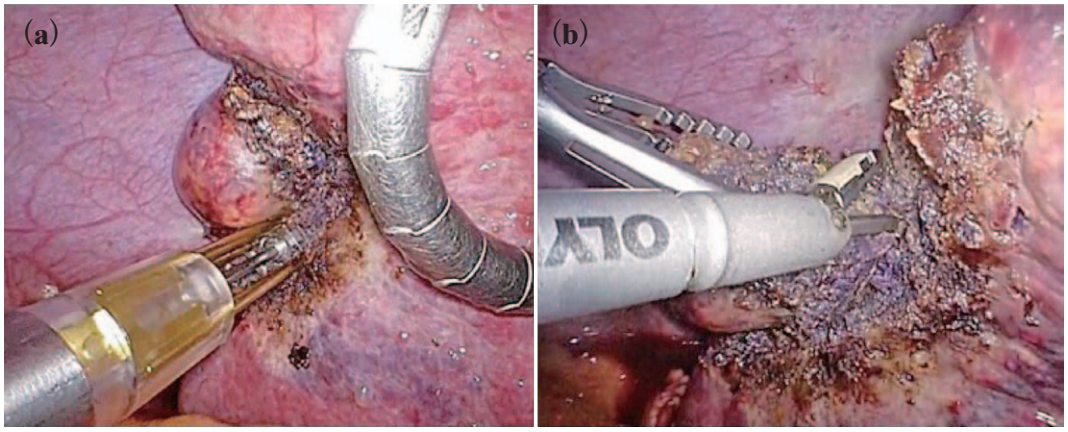

Fig. 1. Intraoperative findings. (a) The Habib 4X (AngioDynamics) was inserted into the cirrhotic liver parenchyma for coagulation and sealing of blood vessels. (b) The parenchyma was then divided with an Ultracision Harmonic Scalpel (Ethicon, Somerville, NJ, USA)

Procedure

Preoperative image simulation was performed using the Synapse Vincent volume analyzer (Fujifilm Medical Co., Ltd., Tokyo, Japan), a three-dimensional analysis system for optimal planning of port placement and enhanced visualization of vessels, bile ducts, and tumors. EH was performed according to previously described procedures [19, 20]. The PM was not used in any of the patients undergoing precoagulation, but we were ready to implement it in case of unexpected intraoperative bleeding during the LH. EH was performed using microwave coagulation therapy (Microtase ; Alfresa Pharma, Osaka, Japan) or RFA (Habib 4X bipolar resection device ; AngioDynamics, Latham, NY, USA). Parenchymal transection was performed using an Ultracision Harmonic Scalpel (Ethicon, Somerville, NJ, USA) after precoagulation. The operative findings are shown in Figure 1.

Results

RFA precoagulation was performed in seven patients, whereas microwave coagulation therapy was performed in four patients. The mean operation time was 156 min (range, 80–310 min), with a mean blood loss of 73 g (range, 5–200 g). No patients underwent the PM or required intraoperative transfusion, and there were no intraoperative complications or conversions to laparotomy. All patients showed improved liver function parameters on postoperative days 1 and 5, although two patients developed postoperative complications comprising Clavien-Dindo grade Ⅲ postoperative bleeding in one case and Clavien-Dindo grade Ⅱ spontaneous bacterial peritonitis (SBP) in the other. The patients' operative characteristics and short-term outcomes are shown in Tables 2 and 3, respectively.

Discussion

Minimally invasive hepatectomy is a growing field of research, with some studies promoting the feasibility of LH in patients with cirrhosis [21, 22]. In the present study, EH without the PM was performed in 11 patients with cirrhosis after precoagulation, and only slight intraoperative

bleeding occurred. This series offers valuable data regarding certain technical modifications that prevent ischemic injury in patients with cirrhosis.

Intraoperative bleeding makes endoscopic surgery difficult and increases the rate of conversion from EH to laparotomy. Cirrhosis increases the risk of hemorrhage, and various hemostatic methods, techniques, and devices are needed to reduce bleeding and increase safety during EH.

Herein, we described a method for reducing blood loss using precoagulation devices before parenchymal transection, although achieving parenchymal division with only slight bleeding during EH remains difficult in patients with cirrhosis. Many liver surgeons perform the PM to reduce intraoperative bleeding ; however, the risk of bleeding remains in patients with liver cirrhosis because they are more susceptible to ischemia-reperfusion injury[12]. The present study investi-

Table 2. Operative outcomes of patients who underwent endoscopic hepatectomy for hepatocellular carcinoma

Variable	n = 11
Technique, n	
Thoracoscopic hepatectomy	2
Laparoscopic hepatectomy	9
Total operative time in min, mean (range)	156 (80-310)
Intraoperative blood loss in g, mean (range)	73 (5-200)
Conversion to open surgery, n	0
Pringle maneuver, n	0
Precoagulation by MCT/RFA, n	3/8
Intraoperative transfusion, n	0
Pathological diagnosis, n	
Hepatocellular carcinoma	11
Tumors, mean (range)	1.1 (1-2)
Size of largest tumor in mm, mean (range)	27.6 (7-90)
R0/R1 resection, n (%)	10 (1)
Postoperative laboratory data, postop day 1/5, mean (range)	
Total bilirubin (mg/dl)	1.21 (0.7-1.9) / 1.08 (0.6-1.5)
Aspartate transaminase (U/l)	179 (81-457) / 42 (33-74)
Alanine transaminase (U/l)	116 (55-266) / 79 (49-173)
Prothrombin time (%)	70 (63-85) / 69 (56-83)

Table 3. Postoperative outcomes of patients who underwent endoscopic hepatectomy for hepatocellular carcinoma

Variable	n = 11
Complications	
Postoperative bleeding, n	1
Spontaneous bacterial peritonitis, n	1
Clavien-Dindo grade of worst complication	
None/Grade Ⅰ/Ⅱ/Ⅲ/Ⅳ/Ⅴ	9/0/1/1/0/0
Hospital stay in days, mean (range)	13.2 (7-33)

gated the hypothesis that precoagulation and no PM is a safe alternative for reducing the risk of ischemia-reperfusion injury during cirrhotic parenchymal transection.

RFA with precoagulation is one of the most commonly used techniques in the clinical treatment of hepatocellular carcinoma. Described for hepatectomy in 2002 by Weber *et al*[13], RFA facilitates resection of the tumor itself and seals the vessels and bile ducts, promoting a nearly bloodless hepatectomy[23], although a few controversial studies maintained that RFA is not completely safe in patients with poor hepatic functional reserve or cirrhosis[24,25]. In response to the controversy, a new RFA device was developed specifically for LH, the Habib 4X[14]. Several studies subsequently confirmed the benefits of RFA-assisted hepatectomy for reducing blood loss[15,16], and this technique was recently recommended for patients with cirrhosis[17,18]. Some studies have further suggested that RFA-assisted hepatectomy without the PM can minimize the risk of ischemia-reperfusion injury of the remnant cirrhotic liver with only minor liver injury[17,26]. Additionally, laparoscopic surgery has some benefits over open surgery. Postoperative ascites is the most frequent and important complication of hepatectomy, especially open hepatectomy, in patients with cirrhosis[27], albeit occurring at a lower frequency than in open hepatectomy[28]. Mechanisms have been proposed for the reduced incidence of postoperative ascites in LH, including preservation of the abdominal wall collateral circulation by avoiding long abdominal incisions and muscle division, as well as preservation of the round ligament, which may contain significant collateral veins. Other possibilities, including less mobilization and manipulation of the liver during laparoscopic procedures, might reduce liver trauma[29], limit lymphatic channel divisions[30], and lower intraoperative fluid requirements. The low liver failure rate in LH could also result from the same mechanisms. Therefore, the optimal approach for patients with cirrhosis is safe EH with precoagulation devices and no use of the PM.

The present study showed a mean operative time of 156 min (range, 80–310 min) and mean blood loss of 73 g (range, 5–200 g). In previous studies, the frequency of PM use reduced with precoagulation[14–17], and it was not needed at all during this study. RFA-assisted hepatectomy also significantly reduces intraoperative blood loss and the rate of intraoperative blood transfusions[14,15,17,18]. In our cohort, no patients required an intraoperative blood transfusion, but one patient required a blood transfusion for postoperative bleeding early on the day of the operation. This patient showed signs of postoperative bleeding (decreasing blood pressure and hemoglobin concentration), and hemorrhagic ascites was collected. Bleeding from vessels on the resected surface found during the operation was ablated and a fibrin-coated collagen fleece (Tachocomb; Nycomed, Roskilde, Denmark) was applied to the resected surface during laparoscopic surgery. The patient's recovery was uneventful. The main reasons for postoperative bleeding were the positive pressure of a carbon dioxide pneumoperitoneum and control of the central venous pressure. This procedure masks the inhibition of intraoperative bleeding compared with open surgery. Patients with cirrhosis should therefore be monitored for hemostasis to reduce the pressure of carbon dioxide pneumoperitoneums and raise the blood pressure before converting or stopping the laparoscopy. Apart from this case, we recorded no postoperative bleeding among the patients undergoing LH with precoagulation.

As in other studies, the alanine transaminase (ALT) and aspartate transaminase (AST) levels were measured postoperatively to assess the extent of hepatic damage to the remnant liver. RFA-assisted hepatectomy patients showed significantly higher serum ALT levels than did those undergoing non-RFA-assisted hepatectomy ; moreover, RFA-assisted hepatectomy can further damage the cirrhotic liver[21]. However, the AST and ALT levels quickly improved in the present study, and the lack of PM might have contributed to the absence of severe hepatic damage.

One patient developed postoperative SBP. *Enterococcus faecium* was detected in the collected ascites. RFA-assisted hepatectomy due to necrotic remnant tissue on the surface of the resected area might have facilitated microbial growth leading to infection. Our one case of SBP might have occurred because liver tissues subjected to coagulative necrosis are prone to infection. In patients with infection secondary to ischemia-reperfusion of the liver by the PM, an increased warm ischemia time results in the production of a large volume of inflammatory cytokines. This is considered to induce injury to liver cells and hepatic sinusoidal endothelial cells, especially in immunosuppressed patients[11].

In summary, EH with precoagulation and without the PM is feasible. Hepatectomy using precoagulation could help to transect cirrhotic parenchyma with only slight intraoperative bleeding. Additionally, precoagulation enables EH without the PM in patients with cirrhosis and might help to avoid ischemic injury induced by the PM. We propose that precoagulation may serve as a standard technique for EH with cirrhosis, and further studies with higher statistical power are warranted.

Acknowledgments

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Conflict of Interest

All authors declare that they have no conflict of interest.

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