# IV 研究成果の刊行物・別冊

### ORIGINAL ARTICLE

# Efficacy of occlusion of hepatic artery and risk of carbon dioxide gas embolism during laparoscopic hepatectomy in a pig model

Kenji Makabe • Hiroyuki Nitta • Takeshi Takahara • Yasushi Hasegawa • Shoji Kanno • Satoshi Nishizuka • Akira Sasaki • Go Wakabayashi

© 2014 Japanese Society of Hepato-Biliary-Pancreatic Surgery

#### **Abstract**

Background The important point in safely performing laparoscopic hepatectomy (LH) is to control bleeding. The aims of this study were: (i) to assess the bleeding reduction effect by occlusion of the hepatic artery in LH; and (ii) to evaluate the risk of carbon dioxide (CO<sub>2</sub>) gas embolism (GE) in the case of high pneumoperitoneum (PP).

Methods Nine piglets underwent laparoscopic left medial lobe and left lateral lobe resection, receiving either occlusion of the hepatic artery (hepatic artery clamping group: HACG, n=9) or no occlusion (hepatic artery declamping group: HADCG, n=9) using a PP of 15 mmHg. In addition, we observed changes in hemodynamics induced by PP. The state of GE was observed using transesophageal echocardiography (TEE) during LH (n=8). GE was graded as grade 0 (none), grade 1 (minor), and grade 2 (major).

Results The HACG had significantly less bleeding compared to the HADCG (P < 0.01). During LH, four animals showed grade 1 (37.5%) and one animal showed grade 2 (12.5%) GE at 15 mmHg. At 20 mmHg, all animals showed grade 2 (100%) GE.

Conclusion The occlusion of the hepatic artery in LH reduces blood loss. The control of bleeding from the hepatic vein is feasible with a high PP, but there is a possibility of GE.

**Keywords** Carbon dioxide gas embolism · Hemodynamics · Hepatic artery occlusion

K. Makabe · H. Nitta (☒) · T. Takahara · Y. Hasegawa · S. Kanno · S. Nishizuka · A. Sasaki · G. Wakabayashi
Department of Surgery, Iwate Medical University School of
Medicine, 19-1 Uchimaru, Morioka, Iwate 020-8505, Japan
e-mail: hnitta@iwate-med.ac.jp

#### Introduction

In recent years, the use of laparoscopic hepatectomy (LH) has spread rapidly due to improvements in the procedure and the development of relevant instruments. Anatomical liver resection, including hemihepatectomy, is currently feasible with laparoscopy [1–3], and donor hepatectomy for living donor liver transplantation is also performed laparoscopically at experienced facilities [4]. The most important point in safely performing these surgical procedures is bleeding control, and techniques, such as precoagulation of the liver parenchyma with radiowaves or microwaves [5] and the Pringle maneuver [6], are often used.

A recent clinical report showed that, in laparotomic hepatectomy of ruptured hepatocellular carcinoma (HCC) [7] and giant liver hemangioma, continuous clamping of the hepatic artery proper using the Pringle maneuver reduced intraoperative bleeding [8].

In LH, bleeding from the hepatic vein and portal vein occurs with the elevation in intra-abdominal pressure caused by pneumoperitoneum (PP) [9–11], and thus a reduction of bleeding is needed. It is predicted that bleeding from the transected surface can be controlled by clamping the hepatic artery proper, which has a higher pressure than that by PP; however, no experimental investigations have tested this hypothesis.

Additionally, it has been reported that the risk of carbon dioxide (CO<sub>2</sub>) gas embolism (GE) rises with increased PP [12–16]. For surgical procedures, such as right hemihepatectomy, CO<sub>2</sub> inflow from vascular holes that are inadvertently created by injuries to the blood vessels is a concern. However, there are also clinical reports that show that LH can be safely performed at high PP (18–20 mmHg), indicating that the risk of GE is controversial.

Using a pig model, the bleeding reduction effect of hepatic artery clamping during LH was investigated, and the elevated PP-induced changes in hemodynamics, including central venous pressure (CVP), portal venous pressure (PVP), hepatic venous flow (HVF), and portal venous flow (PVF), were simultaneously observed. The risk of GE caused by high PP was also evaluated by monitoring gas within the atria with transesophageal echocardiography (TEE) and blood gas analysis.

#### Materials and methods

# Animal preparation

Domestic male pigs with a mean body weight of 35.2 kg (range 34-36 kg) were used in this study. The animals fasted for 24 h with access to water ad libitum until immediately prior to anesthesia induction. A mixture of anesthesia composed of medetomidine hydrochloride, butorphanol tartrate, and midazolam was administered via intramuscular injection. Once the animals were intubated, the anesthesia was maintained with isoflurane inhalation. For intraoperative fluid resuscitation, Ringer's lactate 5 mL/kg per h was infused intravenously to the dorsal vein of the left foot. The animals were in the supine position and maintained on a mechanical ventilator at a tidal volume of 10 mL/kg with a respiratory rate of 20/min. To monitor the intraoperative vital signs, the right ear artery was cannulated to continuously monitor the arterial pressure with an ECG monitor (DASH3000, GE Yokogawa Systems, Tokyo, Japan), and a CV catheter (Single lumen 16 G × 60 cm, Covidien, Mansfield, MA, USA) was inserted into the right external jugular vein to measure CVP. PVP was measured by performing a laparotomy of the upper abdomen and by inserting a catheter (Single lumen 16 G × 60 cm, Covidien) from the splenic vein to the hepatic portal region. For GE monitoring, a TEE probe (ProSound 4000SV, Phased Array Sector Probe, Aloka, Tokyo, Japan) was conducted, and the bubbles in the right atria were recorded over time.

# Hemodynamics

Nine pigs were used in this experiment. Prior to LH, at PPs of 0, 5, 10, and 15 mmHg, mean arterial pressure (MAP, mmHg), CVP (mmHg), and PVP (mmHg) were measured. The hepatic venous diameter (HVD, mm), the portal venous diameter (PVD, mm), the hepatic venous velocity (HVV, cm/s), and the portal venous velocity (PVV, cm/s) were recorded using ultrasound (Pro Focus Ultra View 2202, Transducer 8666, BK Medical, Peabody, MA, USA). HVD was measured at the right hepatic vein, and PVD was measured at the umbilical portion (UP). Based on the measured

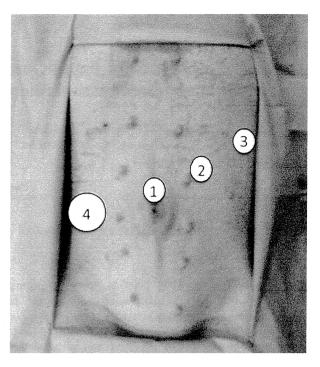


Fig. 1 Schema of port placement on the pig ventral body surface. 1: Pneumo Sleeve site; 2,3: 12 mm trocar; 4: Lap disc for hand assist

blood vessel diameters and blood flow velocities, the blood flows (HVF and PVF, mL/min) were calculated using the following equation:

 $F = \pi \times 1/2 \times D/2 \times V \times 60 \text{ mL/min}$ 

## Bleeding

Hand-assisted LH was performed by a surgeon with extensive experience in this procedure. Trocars for LH were positioned as shown in Figure 1. To clamp the hepatic artery, an incision was made to the hepatoduodenal ligament to tape the common biliary duct and the hepatic artery proper except for the portal vein. LH was performed on the left lobe of the liver (left medial lobe and left lateral lobe) on the pigs that either underwent clamping of the hepatic artery (hepatic artery clamping group, HACG: n = 9) or did not undergo clamping (hepatic artery declamping group, HADCG: n =9). Resection of the two left lobes of the liver was performed, alternating between the groups (i.e., the first case involved the left medial lobe of the HACG and the left lateral lobe of the HADCG, and the second case involved the left lateral lobe of the HACG and the left medial lobe of the HADCG). At the time of liver dissection, the PP was 15 mmHg and the dissection duration was 3 min. The hepatic artery was occluded in the entire period of hepatectomy in the HACG. The liver was resected with sharp scissors at a section approximately 5 cm from the

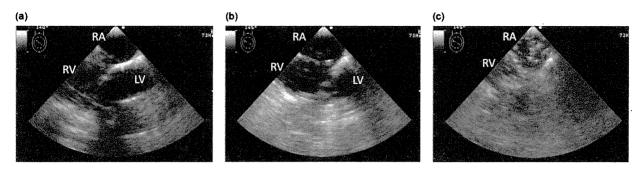


Fig. 2 Examples of definitions of gas embolism (GE) Grade 0 (a), Grade 1 (b), Grade 2 (c). (a) The right outflow tract of the heart (ROT) is visualized by transesophageal echocardiography (TEE); (b) An arrow indicates a gas bubble seen as a white round spot; (c) An arrow indicates a compact mass of gas bubbles filling ROT. LV left ventricle, RA right atrium, RV right ventricle

edge of the liver. Bleeding during this procedure was measured, and the resected liver, which was collected intraabdominally in a plastic bag, was weighed. In order to prepare for the next hepatectomy, Salient SH2.0 (Tissue LINK, Salient Surgical Technologies, Portsmouth, NH, USA) was used on the transected surface to thoroughly stop the bleeding after hepatectomy of one lobe.

### CO<sub>2</sub> gas embolism model

This experiment was performed on eight pigs after LH. The parenchyma surrounding the hepatic vein was sharply resected, such that a 5-mm hole in the blood vessel was formed on the hepatic vein. The state of GE was also observed using TEE during LH. The time after which PP changed from 15 mmHg to 20 mmHg after LH was set as the baseline (0 min); this was compared with a time point 40 min later. MAP, CVP, pH, heart rate (HR), end-tidal CO<sub>2</sub> (etCO<sub>2</sub>), paO<sub>2</sub>, and paCO<sub>2</sub> were the measurement parameters. For blood gas analysis, we used i-STAT analyzer 300F. We also recorded (on DVD) and classified the occurrences of bubbles within the right atrium during the observation period.

Bubbles were classified according to the following: Grade  $0, \le 5$  bubbles; Grade 1, > 5 bubbles but not filling the right atria; and Grade 2, right atrium completely filled with bubbles (Fig. 2).

#### Statistical analysis

The Wilcoxon signed-rank test was used to analyze the amount of bleeding, resected liver weight, and the clinical data at a PP of 20 mmHg. Consecutive data are represented by the median values (range). MAP, CVP, PVP, HVD, PVD, HVV, PVV, HVF, and PVF were compared with Friedman's test. When significance was shown with Friedman's test, Dunn's multiple comparison test was used for further analy-

sis. P < 0.05 was considered significant. Calculations were performed using commercially available software (JMP version 9.0.0; SAS Institute, Cary, NC, USA).

#### Results

#### Hemodynamics

No changes in MAP or HR were observed at each PP level. PVP increased significantly at PPs of 10 mmHg and 15 mmHg compared to 0 mmHg (P < 0.05) (Fig. 3a). There were no changes in CVP at any of the PP levels (Fig. 3b). The morphology of the right hepatic vein and UP changed with increasing PP (an example is shown in Fig. 4), and these changes were observed in all animals. HVD narrowed, showing a significant decrease at PPs of 10 mmHg and 15 mmHg compared to 0 mmHg (P < 0.05). However, there were no significant changes in PVD or HVV, and PVV also did not show significant changes. HVF and PVF displayed decreasing trends on the graphs, but these changes were not significant.

## Bleeding

No changes in vital signs were observed during LH in either group. The median resected liver weights were 25.2 g (9.2–39.9 g) in the HACG and 26.5 g (15.4–52.1 g) in the HADCG, showing no significant difference between the groups. The HACG had significantly less bleeding compared to the HADCG, as indicated by median bleeding amounts of 10.5 g (5.5–45.5 g) and 40 g (14.7–72.8 g), respectively (P < 0.01) (Table 1).

#### CO<sub>2</sub> gas embolism model

The changes in measurements with increasing PP are shown in Table 2. Arterial pressure, paO<sub>2</sub>, and pH decreased, while

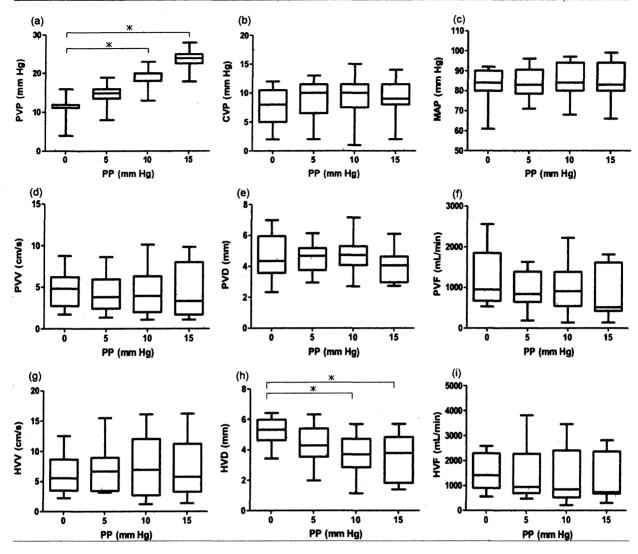


Fig. 3 Box plots showing (a) portal venous pressure (PVP), (b) central venous pressure (CVP), (c) mean arterial pressure (MAP), (d) portal venous velocity (PVV), (e) portal venous diameter (PVD), (f) portal venous flow (PVF), (g) hepatic venous velocity (HVV), (h) hepatic venous diameter (HVD), (i) hepatic venous flow (HVF). Mean (line within box), interquartile range (box) and 10-90th percentile (error bars) are shown. \*P < 0.05 (Friedman test)

CVP, paCO<sub>2</sub>, HR, and end-tidal CO<sub>2</sub> increased (P < 0.05). At a PP of 15 mmHg, four animals had Grade 1 GE (37.5%), and one animal had Grade 2 (12.5%). There were no changes in vital signs caused by GE. At 20 mmHg, all the animals showed Grade 2 GE (100%). Vital signs deteriorated in three of these animals, and two animals developed right heart failure that led to excessive bleeding from the hepatic vein. The three animals with vital sign deterioration had decreased SpO<sub>2</sub>, tachycardia of 150–230 beats/min, increased end-tidal CO<sub>2</sub> to 50–60 mmHg, and decreased blood pressure.

#### Discussion

Liver resection methods with controlled bleeding are essential to promote safe LH, and methods, such as the Pringle maneuver and precoagulation with radiowaves, are known to be useful in this procedure. However, the insertion direction of the needle can be limited in radiowave coagulation under laparoscopy, and there may be difficulties in controlling the bleeding at the time of declamping the blood flow with the Pringle maneuver. In the present study, the changes in hepatic blood flow, CVP, and PVP caused by the

Fig. 4 Morphological changes of portal vein and hepatic vein diameter by ultrasonography

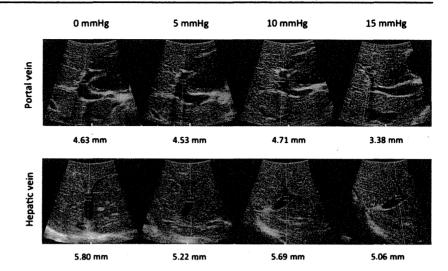


Table 1 Bleeding data and resected liver weight

	HACG	HADCG	P-value
Total bleeding (g)	10.65 (5.5-45.5)	40.0 (14.7–72.8)	0.0039
Resected liver weight (g)	25.2 (9.2–39.9)	26.5 (15.4–52.1)	0.4961

HACG hepatic artery clamping group, HADCG hepatic artery declamping group

Values are median (range). P-values are calculated from a Wilcoxon signed-rank test (P < 0.05)

Table 2 Clinical data baseline (0 min) and 40 min are established. Values are presented as median values

Variables	Baseline (0 min) <sup>a</sup>	40 min <sup>b</sup>	P-value
Mean arterial pressure (mmHg)	68.50 (55–97)	69.50 (52–85)	0.48
Central venous pressure (mmHg)	11.73 (6–16)	17.00 (12-39)	0.01
paO <sub>2</sub> (mmHg)	408 (310–510)	293.5 (99–510)	0.02
paCO <sub>2</sub> (mmHg)	63.85 (51.9–72.5)	83.85 (51.5-130)	0.02
pH	7.34 (7.28–7.41)	7.24 (6.25–7.34)	< 0.01
Heat rate (beat/min)	98 (68–118)	106 (62–170)	0.23
End-tidal CO <sub>2</sub> (mmHg)	43.50 (28–60)	57.50 (34–68)	0.02

<sup>&</sup>lt;sup>a</sup> The time after which PP changed from 15 mmHg to 20 mmHg after LH was set as the baseline (0 min)

P-values are calculated from Wilcoxon signed-rank test (P < 0.05)

increased intra-abdominal pressure during laparoscopic surgery were observed. The circumstances related to the control of bleeding from the hepatic and portal veins were also observed. When it seemed that reduction of PVP and PVF were observed in rising PP, and the same reduction was shown also in hepatic veins, it was speculated that the occlusion of hepatic artery was effective in controlling bleeding. In addition, as a new method to control bleeding, the changes in the amount of bleeding under PP with hepatic artery clamping alone were assessed, and the risk of CO<sub>2</sub> GE at high PP was investigated.

With regards to changes in PVP and PVF, PVP increased significantly to 19 mmHg and 24 mmHg at PPs of

10 mmHg and 15 mmHg, respectively. PVF, while showing decreasing tendencies, did not show significant differences.

Several studies that examined PP and hemodynamics have indicated an increase in PVP and a decrease in PVF. Klopfenstein et al. [17] reported a study on the hemodynamics of pigs at a PP of 15 mmHg. In their study, PVF did not increase significantly. In a clinical study of laparoscopic cholecystectomy, Jakimowicz et al. [9] reported that PVF decreased due to increased PP. While PVP was not mentioned in this study, PVF decreased by 37% at a PP of 7 mmHg and by 53% at a PP of 14 mmHg. In another clinical study of laparoscopic cholecystectomy, Takagi [11] also demonstrated a decreased PVF. Takagi's

<sup>&</sup>lt;sup>b</sup> PP was 20 mmHg

study involved increasing PP in 2-mmHg increments from 0 mmHg to 16 mmHg, this showed that PVF decreased significantly at PP ≥10 mmHg compared to PP of 0 mmHg.

As shown in these studies, PVP elevation and PVF reduction were evident in rising PP. However, in the present study, while PVP exceeded PP when PP was ≥10 mmHg, there were no significant reductions in PVF. PVP, which increased due to compression by PP and PVF, which is an inflow of intestinal blood flow, did not show significant changes. This finding suggests that bleeding from the portal vein cannot be controlled during hepatectomy under high PP conditions.

The CVP and HVF results showed that CVP shifted at a PP <10 mmHg even when it was increased and had a lower value compared to the CVP results at a PP of 15 mmHg during hepatectomy. HVF also showed gradual decreasing tendencies, but the differences were not significant.

The aforementioned pig study by Takagi [11] increased PP from 0 mmHg to 20 mmHg during LH and compared the changes in CVP between the pre-hepatectomy group and the post-hepatectomy group. Both groups showed CVP elevation. In addition, in contrast to previous results reported by others. Bazin et al. [14] also reported their observations with regards to changes in CVP. Their study increased PP to 30 mmHg at a rate of 5 mmHg every minute to observe CVP, but they reported that there were hardly any changes with increased PP. With regards to HVF, Sato et al. [18] used TEE during laparoscopic cholecystectomy and evaluated middle HVF at PPs of 9 mmHg to 12 mmHg, over time. Their results showed a significant decrease in the blood flow of the middle hepatic vein.

As shown in the above studies, there are some aspects that differ regarding CVP and HVF. However, the present results showed that CVP did not increase to the point of exceeding PP, and there were also no changes in blood flow. Therefore, we postulated that bleeding from the hepatic vein can be controlled by PP.

In the present study, bleeding was reduced by continuous hepatic artery flow clamping at the time of liver resection. Judging from the differences in pressures between arterial flow at a high pressure and PP at a lower pressure, it is not feasible to control hepatic artery flow caused by PP. Therefore, the only way to control PP-induced bleeding from the artery is by clamping the hepatic artery.

The hepatic arterial buffer response (HABR) is a well-known physiological function of the liver [19]. It is known to be a mechanism that maintains total hepatic blood flow when PVF decreases and hepatic artery flow consequently increases. The majority of patients with liver cirrhosis are in this state. When PVF reduction is observed under PP, if the body functions such that the hepatic artery flow is increased and the total hepatic blood flow is maintained, then performing hepatic artery clamping during laparoscopic surgery would be *useful* for bleeding reduction. The portal vein and

hepatic artery carry blood to the normal liver, with 20–30% of the inflow from the hepatic artery and 70–80% of the inflow from the portal vein. The present study showed that the difference in bleeding between HACG and HADCG was 25%, which was in agreement with the inflow of the hepatic artery. From these results, we deduced that hepatic artery clamping is a useful procedure.

In addition, because hepatic artery clamping can contribute to bleeding reduction and because its protocol does not entail a hemostasis procedure that is required during declamping in the Pringle maneuver, shorter surgical time can be expected. Xia et al. showed that, in laparotomic hepatectomy of ruptured HCC, continuous clamping of the hepatic artery proper using the Pringle maneuver (study group) reduced intraoperative bleeding less than intermittent Pringle maneuver (control group). Their findings showed that there was no significant difference in hepatic function tests (aspartate transaminase, alanine aminotransferase, total bilirubin) between the two groups. However, their study showed that the disease-free survival in the study group was significantly better than the control group. They stated that this might be related to the patients in the study group having less blood loss and less blood transfusion [7]. Hepatic function tests did not proceed in our study because our study was performed on the same individual pigs. However, it seems from our research finding and their report that the procedure of hepatectomy, which damages the liver, can contribute to reduction in postoperative hepatic failure. We considered a comparative investigation including the Pringle maneuver in the present study, but it was not possible because fatal arrhythmia develops when the portal vein is clamped in pigs.

There are several previous reports of animal experiments concerning PP and GE [12-16]. In a clinical report, Buell et al. [1] used a PP of 18 mmHg to 20 mmHg in major venous bleeding. They stated that the high-risk factor for GE development was related to the patency of the foramen oval. In the present study, five animals showed GE during LH (PP: 15 mmHg), with four animals (37.5%) classified as Grade 1 and one animal (17.5%) classified as Grade 2. The bleeding from the exposed hepatic vein was controlled, but the blood flowing in and out into the blood vessel was observed; thus, we postulated that there was an inflow of gas into the hepatic vein. At a PP of 20 mmHg, all five animals developed Grade 2 GE. Bleeding from the hepatic vein was controlled, and the blood flowing in and out, as observed at a PP of 15 mmHg, was not evident at this PP. Due to the effects of PP and GE, the blood gas analysis at 40 min showed that both pO2 and pH were significantly decreased (P < 0.01). Particularly noteworthy is the finding that the CVP was not different before and after LH at a PP of 15 mmHg (median 11 mmHg), but was significantly increased at a PP of 20 mmHg (median 17 mmHg) (P <

0.01). This increase was considered to be due to right heart failure caused by gas lock (systolic dysfunction of the heart due to pulmonary infarction).

We assessed several reports regarding CVP and PP and found that Eiriksson et al. [15] studied GE at a high PP of 16 mmHg (Group H: n = 8) and at a PP of 8 mmHg (Group L: n = 8), showing that GE was significantly higher in Group H. Jayaraman et al. [16] studied three groups that had different PPs and CVPs (Group 1: high PP, low CVP; Group 2: normal PP, normal CVP; Group 3a: high PP, normal CVP; and Group 3b: normal PP, low CVP), and they demonstrated that one animal in Group 1 had hypotension. Based on the results of the present study and the findings from these reports, the fatality risk of GE appears to increase when the pressure difference between PP and CVP becomes greater. In the present study, the median of CVP at PP of 20 mmHg increased 17 mmHg for right heart failure, and when the pressure difference between PP and CVP become 9-10 mmHg, we expected that the fatality risk of GE was increased. Otsuka et al. [20] reported at the Louisville International Consensus Meeting in 2008 [21] that a clear recommendation of optimal PP for LH cannot be made, and they summarized an article concerning experimental and clinical studies of major liver resection with regards to PP and GE. They concluded that the relationship between PP and CVP should be taken into consideration to reduce the risk of GE, which is a view that is similar to ours.

In conclusion, bleeding during LH appears to be reduced by using the hepatic artery clamping procedure. PVP increased beyond PP, and PVF did not decrease significantly, indicating that PP-induced bleeding from the portal vein cannot be controlled. Bleeding from the hepatic vein can be controlled under high PP conditions, but this may induce GE.

# Conflict of interest None declared.

Author contribution Study design: Kenji Makabe, Hiroyuki Nitta and Go Wakabayashi. Acquisition of data: Kenji Makabe, Hiroyuki Nitta, Yasushi Hasegawa, Takeshi Takahara, Shoji Kanno. Analysis and interpretation: Kenji Makabe, Hiroyuki Nitta, Satoshi Nishizuka. Manuscript drafted by: Kenji Makabe, Hiroyuki Nitta, Satoshi Nishizuka, Akira Sasaki. Statistical advice: Satoshi Nishizuka.

#### References

- Buell JF, Koffron AJ, Thomas MJ, Rudich S, Abecassis M, Woodle ES. Laparoscopic liver resection. Am Coll Surg. 2005;200:472-80.
- Vibert E, Perniceni T, Levard H, Denet C, Shahri NK, Gayet B. Laparoscopic liver resection. Br J Surg. 2006;93:67–72.
- Nitta H, Sasaki A, Otsuka Y, Tsuchiya M, Kaneko H, Wakabayashi G. Impact of hybrid technique on laparoscopic major hepatectomies. J Hepatobiliary Pancreat Sci. 2013;20:111– 13.

- Koffron AJ, Kung R, Baker T, Fryer J, Clark L, Abecassis M. Laparoscopic-assisted right Lobe Donor Hepatectomy. Am J Transplant. 2006;6:2522-5.
- Akyilidiz HY, Morris-Stiff G, Aucejo F, Fung J, Berber E. Techniques of radiofrequency-assisted precoagulation in laparoscopic liver resection. Surg Endsc. 2011;25:1143-7.
- Zhen ZJ, Lau WY, Wang FJ, Lai EC. Laparoscopic liver resection for hepatocarcinoma in the left liver: pringle maneuver versus tourniquet method. World J Surg. 2010;32:314–19.
- Xia F, Lau XY, Qian D, Ma K, Li X, Bie P. Continuous occlusion
  of hepatic artery proper for prevention of blood loss in partial
  hepatectomy for ruptured hepatocellular carcinoma: a casematched comparative study. Ann Surg Oncol. 2011;18:1638-43.
- Xia F, Leu XY, Cheng Qian C, Wang S, Ma K, Rie P. Surgical treatment of giant liver hemangiomas: enucleation with continuous occlusion of hepatic artery proper and intermittent Pringle maneuver. World J Surg. 2010;34:2162-7.
- Jakimowicz J, Stultiens G, Smulders F. Laparoscopic insufflation of the abdomen reduces portal venous flow. Surg Endosc. 1998:12:129-32.
- Yoshida M, Ikeda S, Sumitani D, Takakura Y, Yoshimitsu M, Shimomura M, et al. Alterations in portal vein blood pH, hepatic function, and hepatic histology in a porcine carbon dioxide pneumoperitoneum model. Surg Endosc. 2010;24:1693-700.
- Takagi S. Hepatic and portal vein blood flow during carbon dioxide pneumoperitoneum for laparoscopic hepatectomy. Surg Endosc. 1998;12:427-31.
- Fors D, Eiriksson K, Arvidsson D, Rubertsson S. Gas embolism during laparoscopic liver resection in a pig model: frequency and severity. Br J Anesth. 2010;105:282-282.
- Schmandra TC, Mierdl S, Bauer H, Gutt C, Hanisch E. Transesophageal echocardiography shows high risk of gas embolism during laparoscopic hepatic resection under carbon dioxide pneumoperitoneum. Br J Surg. 2002;89:870-6.
- Bazin JE, Gillart T, Rasson P, Conio N, Aigouy L, Schoeffler P. Haemodynamic conditions enhancing gas embolism after venous injury during laparoscopy: a study in pigs. Br J Anesth. 1997; 78:570-5.
- Eiriksson K, Fors D, Rubertsson S, Arvidsson D. High intraabdominal pressure experimental laparoscopic liver resection reduces bleeding but increases the risk of embolism. Br J Surg. 2011;98:845-52.
- Jayaraman S, Khakhar A, Yang H, Bainbrige D, Quan D. The association between central venous pressure, pneumoperitoneum, and venous carbon dioxide embolism in laparoscopic hepatectomy. Surg Endosc. 2009;23:2369-73.
- Klopfenstein CE, Morel DR, Clergue F, Pastor CM. Effects of abdominal CO<sub>2</sub> insufflation and changes of position on hepatic blood flow in anesthetized pigs. Am J Physiol. 1998;275:H 900– 905.
- Sato K, Kawamura T, Wakusawa R. Hepatic blood flow and function in elderly patients undergoing laparoscopic cholecystectomy. Aneth Analg. 2000;90:1198–202.
- Lautt WW. The 1995 Ciba-Geigy Award Lecture: Intrinsic regulation of hepatic blood flow. Can J Physiol Pharmacol. 1996;74: 223–33.
- Otsuka Y, Katagiri T, Ishii J, Maeda T, Kubota Y. Tamura A, et al. Gas embolism in laparoscopic hepatectomy: what is the optimal pneumoperitoneal pressure for laparoscopic major hepatectomy? J Hepatobiliary Pancreat Sci. 2013;20:137-40.
- Buell JF, Cherqui D, Geller DA, O'Rourke N, Iannitti D, Dagher I, et al. The international position on laparoscopic liver surgery. The Louisville statement, 2008. Ann Surg. 2009;250: 825-30.

#### CASE REPORT

# Pure laparoscopic posterior sectionectomy for liver metastasis resulting from choroidal malignant melanoma: A case report

Akira Umemura, Hiroyuki Nitta, Akira Sasaki, Takeshi Takahara, Yasushi Hasegawa & Go Wakabayashi

Department of Surgery, Iwate Medical University, Morioka, Japan

#### Keywords

Choroidal melanoma; laparoscopic liver resection; liver metastasis

#### Correspondence

Akira Umemura, Department of Surgery, Iwate Medical University, 19-1 Uchimaru, Morioka 020-8505, Japan.

Tel: +81 19 651 5111 Fax: +81 19 651 7166

Email: aumemura@iwate-med.ac.jp

Received: 22 February 2013; revised 25 April 2013; accepted 7 May 2013

DOI:10.1111/ases.12043

#### **Abstract**

Liver metastases resulting from primary choroidal malignant melanomas occur frequently and have a poor prognosis. As a result of advancements in multi-disciplinary approaches, life expectancy can be increased when R0 resection is possible. Herein we report the surgical outcomes of pure laparoscopic posterior sectionectomy (PLPS) in a patient with a solitary liver metastasis resulting from choroidal malignant melanoma. The subject was a 46-year-old Japanese man who had received radiotherapy for primary right choroidal malignant melanoma 2 years before presenting at our hospital; he subsequently underwent ophthalmectomy as a result of the relapse. During follow-up, CT revealed a metastatic lesion in the liver S7, and interventional treatments were performed sequentially. The lesion still showed a tendency to enlarge, so we performed PLPS. On postoperative day 7, the patient was discharged from the hospital, and he started to receive adjuvant chemotherapy 2 weeks after PLPS. Although PLPS is deemed to be difficult for lesions in the upper part or posterior segment of the liver, we performed this modality safely.

#### Introduction

Malignant melanoma can occur in any melanocytes-containing organ of the body. It metastasizes easily either lymphogenously or hematogenously; thus, it progresses rapidly and it associated a poor prognosis (1). Usually, lymphogenous metastases occur in malignant melanomas originating in the skin, whereas hematogenous metastases occur in those originating in the eye and are then confined to the liver, in particular. Liver metastases of malignant melanomas were previously considered to have a poor prognosis. However, as a result of advancements in multidisciplinary approaches to cancer treatment, R0 resection of liver metastases has been demonstrated to increase life expectancy (2,3).

Laparoscopic liver resections have dramatically advanced in recent years, although it remains a somewhat demanding modality for resection of lesions in the upper right lobe or for segmental resection such as posterior sectionectomy (4). Pure laparoscopic liver resection is therefore associated with concerns about safety and securing surgical margins.

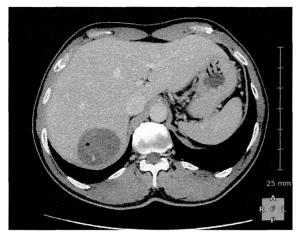
In this report, we describe our experience with pure laparoscopic posterior sectionectomy (PLPS) in a patient with a solitary liver metastasis resulting from primary choroidal malignant melanoma.

#### **Case Presentation**

A 46-year-old Japanese man had been diagnosed with primary right choroidal malignant melanoma 2 years before presenting at our hospital (National Cancer Center Hospital, Tokyo, Japan) and was administered radiotherapy. One year after the melanoma relapsed, he underwent right ophthalmectomy. His histopathological findings were as follows: TNM classification, T4a; tumor thickness, 13 mm; and largest basal tumor diameter, 16 mm, N0, M0. At the 1-year follow-up, CT revealed a liver metastasis measuring 50 mm in S7. Transcatheter arterial infusion and transcatheter arterial chemoembolization were performed sequentially. The lesion enlarged to over 70 mm in diameter and was located in the deep zone of the posterior segment. Therefore, after confirming the absence of extrahepatic lesions, we decided to perform PLPS instead of laparoscopic partial resection (Figure 1).

The patient was placed in the left semilateral position, and we used a five-port technique as in pure laparoscopic

Asian J Endosc Surg 6 (2013) 318–321



**Figure 1** Preoperative abdominal CT. The metastatic melanoma was located in S7. There were no other tumors in the liver or other organs.

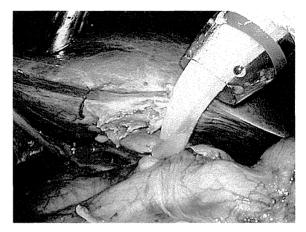
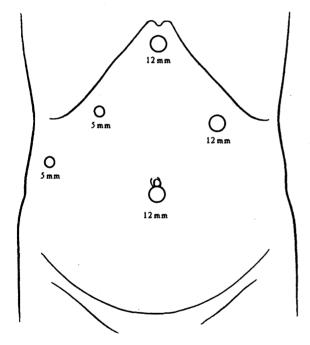


Figure 3 Laparoscopic Pringle's method before hepatic parenchymal transection. A vessel tape was passed around the hepatoduodenal ligament and tied through a soft catheter.



**Figure 2** Port placements for pure laparoscopic posterior sectionectomy. The patient was placed in the left semilateral position. Three 12-mm ports and two 5-mm ports were used.

right lobectomy (Figure 2). During hepatic parenchymal transaction, the upper limit of pneumoperitoneum pressure was set to 8–12 mmHg. Following mobilization of the right lobe and cholecystectomy using laparoscopic coagulating shears (HARMONIC ACE curved shears; Ethicon Endo-Surgery, Tokyo, Japan), intraoperative ultrasonography was performed to confirm the absence of obvious

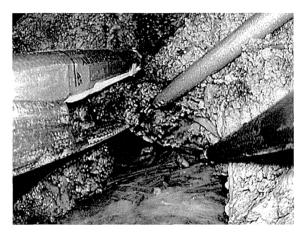


Figure 4 Division of the posterior Glissonian pedicle. The posterior Glissonian pedicle was divided with an endoscopic linear stapler.

multiple lesions and the location of the right hepatic vein in order to determine the surface cutting line of the liver. Hepatic parenchymal transection was performed with an ultrasonic dissector (CUSA EXcel; Integra LifeSciences Corporation, Plainsboro, USA) and a monopolar sealer (TissueLink Endo SH2.0; Salient Surgical Technologies, Minneapolis, USA) using Pringle's method (Figure 3). The right inferior hepatic vein was preserved, and the posterior Glissonian pedicle was divided with an endoscopic linear stapler (ECHELON FLEX 45 mm, open staple height: 2.5 mm; Ethicon Endo-Surgery) after hepatic parenchymal transection (Figure 4). Specimens were obtained from a small suprapubic incision, and the operation was completed. A postoperative histopathological examination revealed liver metastasis of malignant melanoma and negative surgical margins.

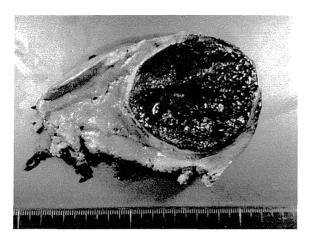


Figure 5 Macroscopic findings of the resected specimen. The resected liver weighed 320 g, and the maximum tumor diameter was 62 mm.

The operating time was 291 min and blood loss was 187 mL; no transfusion was required. The resected liver weighed 320 g, and the tumor size was 62 mm (Figure 5). The drains remained placed for 2 days. On postoperative day 7, the patient was discharged from the hospital, and 2 weeks after PLPS, he was administered adjuvant chemotherapy with dacarbazine, nimustine, cisplatin, tamoxifen, and interferon- $\beta$ . At 6 months of follow-up, the patient was well, with no signs of local or distant recurrences.

# Discussion

Malignant melanoma is usually treated as a systemic disease, especially when it involves remote metastases or recurrent lesions. For liver metastases of malignant melanomas originating in the eye, it is highly likely that micrometastases via systemic circulation have already occurred in other organs. Therefore, local therapy including liver resection is not projected to improve life expectancy (5). As the combination of local therapy including transcatheter arterial infusion or transcatheter arterial chemoembolization with systemic chemotherapy has been demonstrated to increase life expectancy, liver resection is also regarded as an effective therapeutic approach from the viewpoint of surgical oncology, especially if R0 resection is possible (2,3). The 5-year survival for patients with choroidal malignant melanoma ranges from 50% to 70%, and factors affecting results include tumor size, cell type, mitotic activity and local invasion (6). Although patients may benefit from liver metastasis in selected cases, patients with metastatic melanoma have a median survival of 6 months, and fewer than 10% survive after 1 year (2). Kodjikian et al. reported the

median survival time after complete surgical removal of liver metastases followed by postoperative transcatheter arterial infusion in 14 highly selected patients with uveal melanoma (2.3% of the screened population, 22.2% of the metastatic population) was 25 months (7).

In this study, we performed PLPS on a patient with malignant melanoma with a solitary liver metastasis located in S7. Yoon et al. first reported PLPS in 2006 (8). Subsequently, Cho et al. reported that pure laparoscopic liver resection requires abundant experience and sophisticated skills when used for partial resection of lesions in the upper right lobe, subsectionectomy, or sectionectomy (4). To ensure a safe PLPS procedure, some experience with laparoscopic lateral segmentectomy as well as adequate cases of laparoscopic partial resection in the variable location of the liver are needed. We have performed pure laparoscopic liver resection and laparoscopy-assisted liver resection on several occasions and have acquired sufficient experience in this field (9,10). Therefore, we performed PLPS safely in this patient by achieving adequate mobilization of the right lobe under laparoscopy, taking enough measures to reduce bleeding upon liver resection, and selecting appropriate energy devices. In other words, adequate mobilization of the right lobe can provide a wide view of the cut surface of the hepatic parenchyma and thus facilitate division of the Glissonian pedicles or hepatic veins. Furthermore, employing Pringle's method and adjusting both pneumoperitoneum pressure and central venous pressure can help control hemorrhaging during liver resection; laparoscopic coagulating shears, ultrasonic dissectors, and other energy devices can help facilitate hepatic parenchymal transection. However, PLPS is not appropriate for surgeons who lack mature laparoscopic skills, and operating surgeons should consider carefully which patients would be ideal candidates for initial PLPS.

In conclusion, based on our experience with this case, surgical excision may be a useful treatment option in selected cases with solitary, circumscribed liver metastasis resulting from choroidal malignant melanoma. Compared with open hepatectomy, PLPS can have clinical benefits for patients who need adjuvant chemotherapy. Moreover, PLPS represents a potential advantage over other techniques, and this should be evaluated in a comparative study using a large number of patients.

# **Acknowledgments**

The authors would like to thank to Dr Naoko Ito, Dr Shoji Kanno, and Dr Shigeaki Baba for their helpful discussions. The authors have no conflicts of interest to declare.

#### References

- Lee ML, Tomsu K, Von Eschen KB. Duration of survival for disseminated malignant melanoma. Results of a metaanalysis. Melanoma Res 2000; 10: 81-92.
- 2. Herman P, Machado MA, Montagnini AL et al. Selected patients with metastatic melanoma may benefit from liver resection. World J Surg 2007; 31: 171-174.
- Mariani P, Piperno-Neumann S, Servois V et al. Surgical management of liver metastases from uveal melanoma: 16 years' experience at the Institute Curie. Eur J Surg Oncol 2009; 35: 1192-1197.
- Cho JY, Han HS, Yoon YS et al. Outcomes of laparoscopic liver resection for lesions located in the right side of the liver. Arch Surg 2009; 144: 25-29.
- Li Y & McClay EF. Systemic chemotherapy for the treatment of metastatic melanoma. Semin Oncol 2002; 29: 413–426.

- Feldman ED, Pingpank JF, Alexander HR Jr. Regional treatment options for patients with ocular melanoma metastatic to liver. Ann Surg Oncol 2004; 11: 290-297.
- Kodjikian L, Grange JD, Baldo S et al. Prognostic factors of metastases from uveal melanoma. Graefes Arch Clin Exp Ophthalmol 2005; 243: 985-993.
- Yoon YS, Han HS, Choi YS et al. Total laparoscopic right posterior sectionectomy for hepatocellular carcinoma. J Laparoendosc Adv Surg Tech A 2006; 16: 274–277.
- Sasaki A, Nitta H, Otsuka K et al. Ten-year experience of totally laparoscopic liver resection in a single institution. Br J Surg 2009; 96: 274-279.
- Nitta H, Sasaki A, Fujita T et al. Laparoscopy-assisted major liver resections employing a hanging technique: The original procedure. Ann Surg 2010; 251: 450-453.

Well.

#### VIDEO

# Pure laparoscopic right hepatectomy by anterior approach with hanging maneuver for large intrahepatic cholangiocarcinoma

Masahiro Takahashi · Go Wakabayashi · Hiroyuki Nitta · Daiki Takeda · Yasushi Hasegawa · Takeshi Takahara · Naoko Ito

Received: 18 August 2012/Accepted: 24 May 2013/Published online: 30 October 2013 © The Author(s) 2013. This article is published with open access at Springerlink.com

#### Abstract

Background Pure laparoscopic hemihepatectomy is still a challenging procedure. However, it is a minimally invasive liver surgery that leads to rapid recovery [1–5]. Intrahepatic cholangiocarcinoma has a poor prognosis, especially when it occurs with lymph node metastasis [6–8]. We recently had a patient who underwent a pure laparoscopic right hepatectomy and lymph nodes dissection for a large intrahepatic cholangiocarcinoma in the right liver by an anterior approach with hanging maneuver.

Methods Because the tumor was  $77 \times 50$  mm in diameter, mobilization was performed after the devascularization of the right liver. After the division of the right hepatic artery and the right portal vein, short hepatic veins were sealed and divided with a bipolar vessel sealer from the anterior face of the vena cava, followed by the placement of a tape between the liver and the vena cava for hanging. By means of the hanging maneuver, parenchymal transection was performed with minimal blood loss, and the cut surface of the liver became plane.

Results The operation time was 357 min, and the blood loss was 66 ml. A right hepatectomy and complete lymph node dissection adjacent to the hepatoduodenal ligament were performed successfully with a purely laparoscopic

**Electronic supplementary material** The online version of this article (doi:10.1007/s00464-013-3202-2) contains supplementary material, which is available to authorized users.

M. Takahashi  $(\boxtimes)$  · G. Wakabayashi · H. Nitta · D. Takeda · Y. Hasegawa · T. Takahara · N. Ito

Department of Surgery, Iwate Medical University of Medicine, Morioka, Iwate, Japan

e-mail: takahash@iwate-med.ac.jp

G. Wakabayashi

e-mail: gowaka@iwate-med.ac.jp

procedure. The postoperative hospital stay was 10 days. The final diagnosis of the intrahepatic cholangiocarcinoma with distant lymph node metastasis in the hepatoduodenal ligament was pT1N1M0 stage IIIb (International Union Against Cancer criteria).

Conclusions The laparoscopic procedure enabled the patient to have an early discharge and adjuvant chemotherapy of gemcitabine with S1 initiated immediately after discharge. We present a video of the described procedure.

**Keywords** Endoscopy · Hepatic cancer · Surgical technique

**Disclosures** Masahiro Takahashi, Go Wakabayashi, Hiroyuki Nitta, Daiki Takeda, Yasushi Hasegawa, Takeshi Takahara, and Naoko Ito have no conflicts of interest or financial ties to disclose.

Open Access This article is distributed under the terms of the Creative Commons Attribution Noncommercial License which permits any noncommercial use, distribution, and reproduction in any medium, provided the original author(s) and the source are credited.

# References

- Cherqui D, Husson E, Hammoud R, Malassagne B, Stéphan F, Bensaid S, Rotman N, Fagniez PL (2000) Laparoscopic liver resections: a feasibility study in 30 patients. Ann Surg 232:753-762
- Gigot JF, Glineur D, Azagra JS, Goergen M, Ceuterick M, Morino M, Etienne J, Marescaux J, Mutter D, van Krunckelsven L, Descottes B, Valleix D, Lachachi F, Bertrand C, Mansvelt B, Hubens G, Saey JP, Schockmel R, Hepatobiliary and Pancreatic Section of the Royal Belgian Society of Surgery and the Belgian Group for Endoscopic Surgery (2002) Laparoscopic liver resection for malignant liver tumors: preliminary results of a multicenter European study. Ann Surg 236:90-97
- Koffron AJ, Auffenberg G, Kung R, Abecassis M (2007)
   Evaluation of 300 minimally invasive liver resections at a single institution: less is more. Ann Surg 246:385-392

- Nguyen KT, Gamblin TC, Geller DA (2009) World review of laparoscopic liver resection—2,804 patients. Ann Surg 250: 831-841
- 5. Buell JF, Cherqui D, Geller DA, O'Rourke N, Iannitti D, Dagher I, Koffron AJ, Thomas M, Gayet B, Han HS, Wakabayashi G, Belli G, Kaneko H, Ker CG, Scatton O, Laurent A, Abdalla EK, Chaudhury P, Dutson E, Gamblin C, D'Angelica M, Nagorney D, Testa G, Labow D, Manas D, Poon RT, Nelson H, Martin R, Clary B, Pinson WC, Martinie J, Vauthey JN, Goldstein R, Roayaie S, Barlet D, Espat J, Abecassis M, Rees M, Fong Y, McMasters KM, Broelsch C, Busuttil R, Belghiti J, Strasberg S, Chari RS, World Consensus Conference on Laparoscopic Surgery (2009) The international position on laparoscopic liver surgery: the Louisville Statement, 2008. Ann Surg 250:825-830
- Inoue K, Makuuchi M, Takayama T, Torzilli G, Yamamoto J, Shimada K, Kosuge T, Yamasaki S, Konishi M, Kinoshita T, Miyagawa S, Kawasaki S (2000) Long-term survival and prognostic factors in the surgical treatment of mass-forming type cholangiocarcinoma. Surgery 127:498-505
- Uenishi T, Hirohashi K, Kubo S, Yamamoto T, Yamazaki O, Kinoshita H (2001) Clinicopathological factors predicting outcome after resection of mass-forming intrahepatic cholangiocarcinoma. Br J Surg 88:969-974
- Shimada M, Yamashita Y, Aishima S, Shirabe K, Takenaka K, Sugimachi K (2001) Value of lymph node dissection during resection of intrahepatic cholangiocarcinoma. Br J Surg 88: 1463-1466

