Ⅱ　研究成果の刊行に関する一覧表

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雑誌

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Otsuka Y, Katagiri T, Ishii J, Maeda T, Kubota Y, Tamura A, Tsuchiya M, Kaneko H.	Gas embolism in laparoscopic hepatectomy: what is the optimal pneumoperitoneal	J Hepatobiliary Pancreat Sci.	20	137-140	2013
Makabe K, Nitta H, Takahara T, Hasegawa Y, Kanno S, Nishizuka S, Sasaki A, Wakabayashi G.	Efficacy of occlusion of hepatic artery and risk of carbon dioxide gas embolism during laparoscopic	J Hepatobiliary Pancreat Sci.	21	Epub	2014
Umemura A, Nitta H, Sasaki A, Takahara T, Hasegawa Y, Wakabayashi G.	Pure laparoscopic posterior sectionectomy for liver metastasis resulting from	Asian J Endosc Surg.	6	318-321	2013
Takahashi M, Wakabayashi G, Nitta H, Takeda D, Hasegawa Y, Takahara T, Ito N.	Pure laparoscopic right hepatectomy by anterior approach with hanging maneuver for large intrahepatic	Surg Endosc.	27	4732-4733	2013

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Impact of hybrid techniques on laparoscopic major hepatectomies

Hiroyuki Nitta · Akira Sasaki · Yuichiro Otsuka · Masaru Tsuchiya · Hironori Kaneko · Go Wakabayashi

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Abstract
Purpose To assess the types of liver resection, surgical approaches, and surgical outcomes, a questionnaire survey was undertaken at 32 member hospitals of the Japanese Endoscopic Liver Study Group.
Methods/results Laparoscopic liver resections were performed on 837 patients. Major hepatectomy, including trisectionectomy, hemihepatectomy, and sectionectomy, constituted 106 of the cases. Laparoscopic major hepatectomy (LMH) was performed as totally laparoscopic ($n = 8$) (7.5 %), hand-assisted ($n = 4$) (3.8 %), or laparoscopy-assisted ($n = 94$) (88.7 %). None of the 106 patients were converted to open surgery. Complications occurred in 18 (17.0 %) of the 106 patients. One patient (0.9 %) had bleeding, two (1.9 %) had liver failure, six (5.7 %) had bile leakage, two (1.9 %) had pleural effusion, five (4.7 %) had surgical site infection, one (0.9 %) had pneumonia, and one (0.9 %) had acute respiratory distress syndrome. There were no perioperative deaths or gas embolisms.
Conclusion In conclusion, a major hepatectomy using a hybrid technique is safe and feasible.

Keywords Laparoscopy-assisted · Hybrid · Major hepatectomy

H. Nitta (✉) · 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

Y. Otsuka · M. Tsuchiya · H. Kaneko
Division of General and Gastroenterological Surgery, Department of Surgery (Omori), Toho University School of Medicine, Tokyo, Japan

Introduction

Laparoscopic major hepatectomies (LMH) have been reported [1–4]. Compared with liver resection by laparotomy, the incision is much smaller and the degree of body wall damage is reduced. However, because a high degree of proficiency is required, major hepatectomies have not been widespread.

We have already reported on a laparoscopy-assisted major liver resection in 2010 [5]. The liver was mobilized laparoscopically and a parenchymal transection was made by using a hanging technique through a small incision in the right sub-costal or upper middle region. The advantage of this hybrid technique is that it does not require knowledge of any advanced laparoscopic techniques. Therefore, it is acceptable for open liver surgery.

In Japan, every year a questionnaire survey is undertaken by the Japanese Endoscopic Liver Study Group to assess the status of laparoscopic liver surgery [6]. According to the results, there are more laparoscopy-assisted surgeries than totally laparoscopic major liver resections. We report here the results of this survey, which attempted to assess the current status of LMH in Japan.

Subjects and results

To assess the types of operative procedures, surgical approaches, and surgical outcomes, a questionnaire survey was undertaken at 32 member hospitals of the Japanese Endoscopic Liver Study Group in 2009.

The types of liver resections and surgical approaches

Laparoscopic liver resections were performed on 837 patients. The types of liver resection consisted of trisectionectomy ($n = 2$), extended hemihepatectomy ($n = 12$), hemihepatectomy ($n = 70$), sectionectomy ($n = 22$), left lateral sectionectomy ($n = 180$), anatomical segmentectomy ($n = 30$), and non-anatomical wedge resection ($n = 521$) (Table 1). Major hepatectomy, including trisectionectomy, hemihepatectomy, and sectionectomy, constituted 106 of the cases. LMH was performed as totally laparoscopic ($n = 8$) (7.5 %), hand-assisted ($n = 4$) (3.8 %), or laparoscopy-assisted ($n = 94$) (88.7 %) (Table 2; Fig. 1).

Surgical outcomes of LMH

None of the 106 patients were converted to open surgery. Complications occurred in 18 (17.0 %) of the 106 patients.

Table 1 Types of liver resection

	No. of patients
Trisectionectomy	2
Extended hemihepatectomy	12
Hemihepatectomy	70
Sectionectomy	22
Left lateral sectionectomy (LLS)	180
Anatomical segmentectomy (AS)	30
Non-anatomical wedge resection (NAWR)	521
Total	837

Table 2 Types of surgical approach

	No. of patients
Totally laparoscopic ($n = 466$)	
MLR	8
LLS	87
AS	12
NAWR	359
Hand-assisted ($n = 48$)	
MLR	4
LLS	6
AS	2
NAWR	36
Laparoscopy-assisted (hybrid) ($n = 319$)	
MLR	94
LLS	87
AS	16
NAWR	122
Thoracoscopy ($n = 4$)	
NAWR	4
Total	837

MLR included trisectionectomy (extended) hemihepatectomy, and sectionectomy

MLR major liver resection

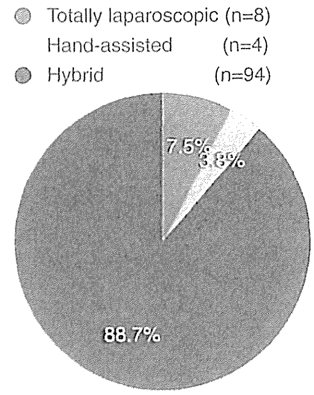

Fig. 1 Major hepatectomy constituted 106 of the cases. LMH was performed as totally laparoscopic ($n = 8$; 7.5 %), hand-assisted ($n = 4$; 3.8 %), or laparoscopy-assisted ($n = 94$; 88.7 %)

Table 3 Surgical outcomes of laparoscopic liver resection

	MLR ($n = 106$)	LLS ($n = 180$)	AS ($n = 30$)	NAWR ($n = 521$)
Conversion to open surgery	0	5	2	12
Complications	18	14	2	38
Bleeding	1	3	0	5
Liver failure	2	0	1	0
Bile leakage	6	4	0	4
Pleural effusion	2	1	0	5
Ascites	0	2	1	14
Liver abscess	0	0	0	1
Surgical site infection	5	4	0	5
Pneumonia	1	0	0	0
Gastrointestinal bleeding	0	0	0	2
Hypercarbondioxidemia	0	0	0	1
Ileus	0	0	0	0
ARDS	1	0	0	1

One patient (0.9 %) had bleeding, two (1.9 %) had liver failure, six (5.7 %) had bile leakage, two (1.9 %) had pleural effusion, five (4.7 %) had surgical site infection, one (0.9 %) had pneumonia, and one (0.9 %) had acute respiratory distress syndrome (Table 3). There were no perioperative deaths or gas embolisms.

Discussion

According to previous reports, when performed by experienced surgeons on selected patients, laparoscopic liver resection may be a safe and feasible option [7, 8]. LMH has not been widely practiced, and this type of resection is difficult if the surgeon does not have the appropriate knowledge and skills for both laparoscopic and liver surgery. The advantage of laparoscopy-assisted (hybrid) LMH is that it does not require knowledge of any advanced laparoscopic techniques; thus, liver surgeons can perform it easily.

A questionnaire survey by the Japanese Endoscopic Liver Study Group showed that many LMH were performed using a hybrid technique rather than being totally laparoscopic, probably to avoid gas embolism. There were no conversions to open surgery and no severe complications. LMH using the hybrid technique was safe and feasible.

In our institution, 299 patients had laparoscopic liver resections between March 1997 and June 2012. Many major hepatectomies were performed using hybrid techniques. However, recently, a major hepatectomy was conducted using totally laparoscopic techniques because the case was difficult and included a high body mass index (BMI) patient who had also undergone chemotherapy. This totally laparoscopic major hepatectomy was safely performed in our institution because we have a lot of experience with assisted hepatectomies.

In conclusion, a major hepatectomy using a hybrid technique is safe and feasible. Furthermore, for training purposes, it serves as a bridge between open and totally laparoscopic hepatectomies.

Appendix: 32 member hospitals of the Japanese Endoscopic Liver Study Group

Iwate Medical University Hospital, Toho University Omori Medical Center, Eiju General Hospital, Oita University Hospital, Osaka Medical College Hospital, Osaka University Hospital, Kitasato University East Hospital, Kyushu University Hospital, St. Marianna University School of Medicine Hospital, Chiba Cancer Center, Jikei University School of Medicine Hospital, Jikei University School of Medicine Kashiwa Hospital, Tokushima University Hospital, Hokkaido University Hospital, Yokoyama Gastrointestinal Hospital, Aichi Medical University Hospital, Kyoto University Hospital, Kumamoto University Hospital, Keio University Hospital, National Cancer Center East Hospital, Shinshu University Hospital, Tokyo Medical and Dental University Hospital, Tokyo Medical University Hachioji Medical Center, Tokyo Women's Medical University Hospital, Nagasaki University Hospital, Nagano Municipal Hospital, Nippon Medical School Hospital, Hiroshima University Hospital, Tokyo University Hospital, Tohoku University Hospital, Dokkyo Medical University Hospital, Akita University Hospital.

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Gas embolism in laparoscopic hepatectomy: what is the optimal pneumoperitoneal pressure for laparoscopic major hepatectomy?

Yuichiro Otsuka · Toshio Katagiri · Jun Ishii · Tetsuya Maeda · Yoshihisa Kubota · Akira Tamura · Masaru Tsuchiya · Hironori Kaneko

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Abstract Laparoscopic hepatectomy (LH) has become popular as a surgical treatment for liver diseases, and numerous recent studies indicate that it is safe and has advantages in selected patients. Because of the magnified view offered by the laparoscope under pneumoperitoneal pressure, LH results in less bleeding than open laparotomy. However, gas embolism is an important concern that has been discussed in the literature, and experimental studies have shown that LH is associated with a high incidence of gas embolism. Major hepatectomies are done laparoscopically in some centers, even though the risk of gas embolism is believed to be higher than for minor hepatectomy due to the wide transection plane with dissection of major hepatic veins and long operative time. At many high-volume centers, LH is performed at a pneumoperitoneal pressure less than 12 mmHg, and reports indicate that the rate of clinically severe gas embolism is low. However, more studies will be necessary to elucidate the optimal pneumoperitoneal pressure and the incidence of gas embolism during LH.

Keywords Laparoscopic hepatectomy · Laparoscopic liver resection · Major hepatectomy · Pneumoperitoneum · Gas embolism

Introduction

Laparoscopic hepatectomy (LH) is a new surgical treatment option for patients with liver disease. In 2008, the Louisville International Consensus Meeting was held to discuss LH and determined that when LH is performed by experienced liver surgeons who are knowledgeable in the use of a laparoscope, it can be a safe and effective procedure for treating liver tumors [1]. Despite the increasing popularity of LH, the procedure is associated with two well-known problems: control of bleeding and the risk of CO_2 gas embolism (gas embolism). Although the problem of gas embolism was discussed at the Louisville International Consensus Meeting, no agreement was reached on concrete recommendations for suitable pneumoperitoneal pressure (PP) during LH [1].

Huscher et al. [2] were the first to report laparoscopic surgery for major hepatectomy, in 1998. However, due to technical difficulties with this procedure, it took many years for suitable operative techniques to be developed. At present, although laparoscopic major hepatectomies can now be performed safely, only a limited number of centers routinely perform them [3–9]. Laparoscopic major hepatectomy is believed to have a higher risk than minor hepatectomy of gas embolism, because of the extensive hepatic transection plane, operative duration, and dissection of large hepatic veins or vena cava.

This article discusses experimental and clinical studies of PP and gas embolism during laparoscopic surgery, especially laparoscopic major hepatectomy.

Risk of gas embolism during laparoscopic surgery

To obtain the operative field for laparoscopic surgery, CO_2 is generally used to create PP, and there are reports of gas embolism for all types of laparoscopic surgery [10–15]. The overall incidence of gas embolism during laparoscopic surgery is considerably low, at approximately 0.15 % [15], and the incidence is only 0.06 % for laparoscopic cholecystectomy

Y. Otsuka · T. Katagiri · J. Ishii · T. Maeda · Y. Kubota · A. Tamura · M. Tsuchiya · H. Kaneko (✉)
Department of Surgery, Toho University Faculty of Medicine, 6-11-1 Omori-nishi, Ota-ku, Tokyo 143-8541, Japan
e-mail: hironori@med.toho-u.ac.jp

Y. Otsuka
e-mail: yotsuka@med.toho-u.ac.jp

[16]. However, when gas embolism does develop, the mortality rate can be as high as 30 % [14, 17]. Thus, although laparoscopic procedures are minimally invasive, they can lead to potentially life-threatening complications.

Because the risk of gas embolism during pneumoperitoneum has always been present in LH due to the unique anatomy of the liver, many studies performed LH with PP minimized in order to avoid the risk of gas embolism [18]. In the animal model, however, any levels of PP can be considered potentially dangerous, and so gasless laparoscopy, either abdominal wall lifting or laparoscopy-assisted surgery, was recommended [9, 19].

Increased pressure to control bleeding in LH

It is believed that the lower blood loss in LH as compared with open hepatectomy (OH) is due to PP and the magnified view offered by laparoscopy. It has been suggested that high PP is occasionally advantageous for hemostasis, and poses few clinical risks because the solubility of carbon dioxide in human plasma at 37 °C is greater than that of air [20]. Several clinical studies of LH also suggested that higher PP was effective in controlling bleeding during liver parenchymal transection [21], and one study used PP ranging from 18 to 20 mmHg [22]. In addition, Jaskille et al. [23] reported that maintenance of constant PP during surgery reduced blood loss in an animal model of liver trauma.

Dissection of major hepatic veins and decreased central venous pressure in major hepatectomy

In major hepatectomy, many authors insist that the hepatic vein must be sufficiently exposed on the surface to be transected during anatomical resection [24]. Furthermore, by maintaining low central venous pressure (CVP), bleeding from blood vessels on the resectioned surface can be minimized [25, 26]. Although there is a risk of air embolism caused by absorption of air into the vena cava through the branches of the hepatic veins during OH [27], the incidence of clinically significant air embolism is low, as lower CVP is commonly used during OH [28]. However, it is assumed that the risk of gas embolism would be enhanced by low CVP combined with high PP.

Experimental studies of laparoscopic major hepatectomy

Schmandra et al. [29] performed left hepatectomies on pigs divided into a totally LH group at a PP of 12 mmHg and an OH group. There was no case of air embolism in the OH group; however, gas embolism developed in all pigs that underwent LH. As operative time increased, the partial pressure of oxygen in arterial blood decreased. The authors later conducted a sililar study using hand-assisted technique and found that the incidence of gas embolism decreased [30].

Eiriksson et al. [31] also performed laparoscopic left hepatectomy on pigs using PPs of 8 and 16 mmHg. Blood loss was significantly lower at the higher pressure; however, the incidence of gas embolism was higher. The authors concluded that close monitoring for gas embolism is necessary when using high pressure; in addition, changes in the systemic circulation, such as mean arterial pressure or pulse rate, are not sensitive or specific for gas embolism except in a very late, fatal phase.

Jayaraman et al. [32] performed hand-assisted laparoscopic left hepatectomies in 3 groups of different PP-to-CVP gradient. In the positive gradient group, PP was normal (14 mmHg) and CVP was decreased to less than 5 mmHg; in the negative gradient group, CVP was normal (10–12 mmHg) and PP was decreased to 7 mmHg; in the neutral gradient group, the pressures were equal (either both at normal levels or both lowered to the reduced levels described above). The authors suggested that the risk of gas embolism increased as the PP-to-CVP ratio increased.

Clinical studies of laparoscopic major hepatectomy

There have been more than fifty English-language reports of laparoscopic major hepatectomy, comprising nearly a thousand cases, up to May 2012. Table 1 shows the characteristics of studies with more than 10 enrolled subjects undergoing laparoscopic major hepatectomy at single centers, with hepatic parenchymal transection under the pneumoperitoneum [3, 6, 8, 33–39]. Studies featuring LH using the laparoscopy-assisted technique, which divide the liver parenchyma through a small laparotomy, are excluded from this result. These reports comprise 477 laparoscopic major hepatectomies involving 3 or more Couinaud's segments. Among the 10 studies, information regarding PP during hepatic parenchymal transection was available in 8 studies. In 6 of these 8 studies, PP was usually maintained at 12 mmHg or lower; the other 2 studies used pressures higher than 12 mmHg. Cannon et al. [37] used pressures of 12–15 mmHg to control bleeding from veins on the surface of the transected liver (including exudative bleeding); however, pressure was not maintained routinely at these high levels. A detailed report by Gayat et al. [6] described that PP was maintained between 8 and 12 mmHg, but before transection of the liver parenchyma, pressure was reduced to the minimum required to maintain a clear operative field (8–10 mmHg), to reduce the risk of gas embolism. Furthermore, to control bleeding from the hepatic veins, the authors reported that it was useful to keep the inferior vena cava in a "half-filled" state (i.e., with visible motion in the vein in response to pulse and respiration). Because of the pressure effects of pneumoperitoneum, CVP readings transduced from a central venous catheter do not accurately reflect actual CVP, which suggests that it is advantageous to maintain both low PP and low CVP.

Three (0.2 %) patients developed gas embolism in this series, but there was no causal relationship between the pressures used and the development of clinically important gas embolisms. The Henri Mondor Hospital Group reported 2 cases (1.72 %) of gas embolism among a total of 166 LH patients. During surgery, there were sudden slight or temporary decreases in end-tidal CO_2 concentration ($ETCO_2$), which were diagnosed to be due to gas embolism. However, there were no complications related to gas embolism during postoperative recovery in either case [36]. Dagher et al. [3] reported a case of gas embolism caused by a tear in the section line of the right hepatic vein. This incident resulted in a transient lowering of blood pressure and was treated by laparoscopic suture.

Dagher et al. [40] also reported 210 cases of laparoscopic major hepatectomy performed at high-volume centers in Western countries; 3 (1.43 %) patients developed gas embolism. All 3 had undergone right hepatectomy, and the embolisms developed during the dissection of the hepatic veins. However, the influence of gas embolism on postoperative morbidity and mortality was not indicated.

Finally, a study of registry data collected during an 8-year period revealed 1 case (0.55 %) of gas embolism without mortality among 182 LHs performed at multiple centers in Spain [41].

Conclusions

Studies of LH procedures performed at experienced high-volume centers found low incidences of gas embolism, but the rates were higher than those for other types of laparoscopic surgery. PP is maintained at less than 12 mmHg in many centers, which appears to be a suitable pressure; however, experimental studies have shown that gas embolism can frequently occur even at such pressures. In addition, careful consideration must be taken of the PP-to-CVP gradient to reduce the risks of gas embolism. It is also important to continue developing safer surgical techniques that avoid hepatic venous injuries and shorten operative time, thus minimizing the duration of PP. Moreover, additional data on peri-operative complications, including available registry information, should be collected to determine the optimal PP and the incidence of gas embolism in LH.

Table 1 Characteristics of studies of laparoscopic major hepatectomy that enrolled more than 10 patients (at single centers)*

References	Years	No. of LH cases	Laparoscopic major hepatectomies		Procedure of LH	Mortality		Morbidity		Pneumoperitoneal pressure during parenchymal transection (mmHg)	Incidence of gas embolism	
			n	%		*n*	%	*n*	%		*n*	%
Dulucq et al. [33]	2005	32	11	34.4	TL	0	0.0	NA	NA	~12	0	0.0
Koffron et al. [8]	2007	300	119	39.7	TL/HA/LA(241/32/27)	NA	NA	28	9.3	NA	NA	NA
Gayat et al. [6]	2007	42	42	100.0	TL	1	2.4	NA	NA	8~10	NA	NA
Topal et al. [34]	2008	109	21	19.3	TL	0	0.0	6	5.5	6~8	NA	NA
Cho et al. [35]	2008	128	36	28.1	TL	1	0.8	22	17.2	~12	0	0.0
Bryant et al. [36]	2009	166	31	18.7	TL/HA (150/16)	0	0.0	25	15.1	~12	2	1.2
Dagher et al. [3]	2009	22	22	100.0	TL	0	0.0	3	13.6	NA	1	4.5
Cannon et al. [37]	2011	300	133	44.3	TL/HA (89/211)	5	1.7	32	10.7	12~15 (temporary)	0	0.0
Choi et al. [38]	2012	30	20	66.7	TL (Robot)	0	0.0	13	43.3	12	NA	NA
Abu Hilal et al. [39]	2012	133	42	31.6	TL	1	0.8	16	12.0	12~14	NA	NA
Total		1262	477	37.2		8	0.6	145	11.5		3	0.2

*Studies performing laparoscopic major hepatectomy only by laparoscopy-assisted technique are excluded

NA not available, *TL* totally laparoscopic procedure, *HA* hand-assisted laparoscopic procedure, *LA* laparoscopy-assisted procedure

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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

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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_2) 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_2) gas embolism (GE) rises with increased PP [12–16]. For surgical procedures, such as right hemihepatectomy, CO_2 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 blood vessel diameters and blood flow velocities, the blood flows (HVF and PVF, mL/min) were calculated using the following equation:

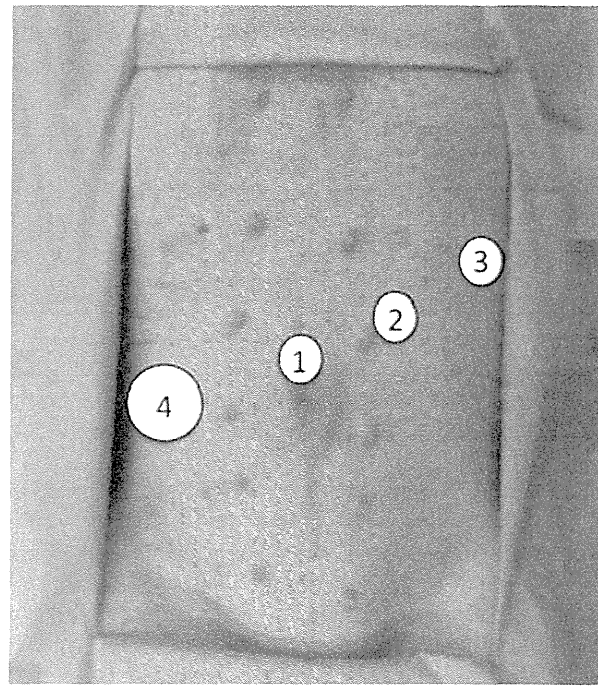

Fig. 1 Schema of port placement on the pig ventral body surface. 1: Pneumo Sleeve site; 2,3: 12 mm trocar; 4: Lap disc for hand assist

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

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

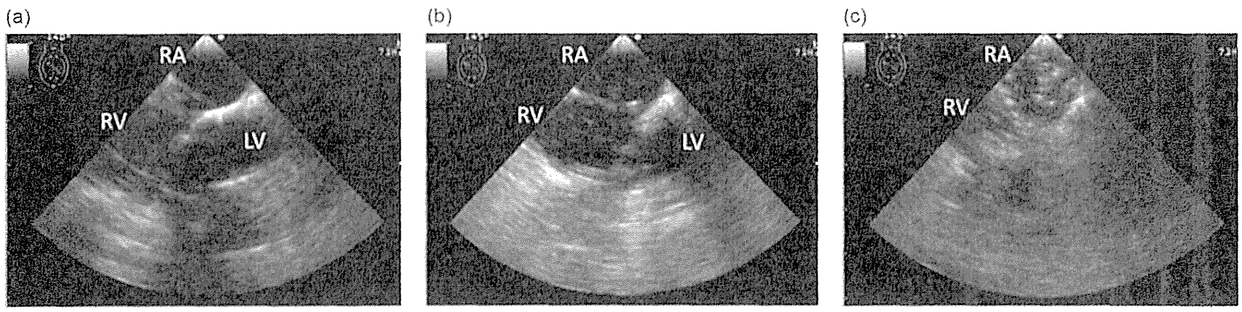

Fig. 2 Examples of definitions of gas embolism (GE) Grade 0 (**a**), Grade 1 (**b**), Grade 2 (**c**). (**a**) The right outflow tract of the heart (ROT) is visualized by transesophageal echocardiography (TEE); (**b**) An arrow indicates a gas bubble seen as a white round spot; (**c**) An arrow indicates 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_2 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_2 ($etCO_2$), paO_2, and $paCO_2$ 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, ≤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 analysis. $P < 0.05$ 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_2 gas embolism model

The changes in measurements with increasing PP are shown in Table 2. Arterial pressure, paO_2, and pH decreased, while

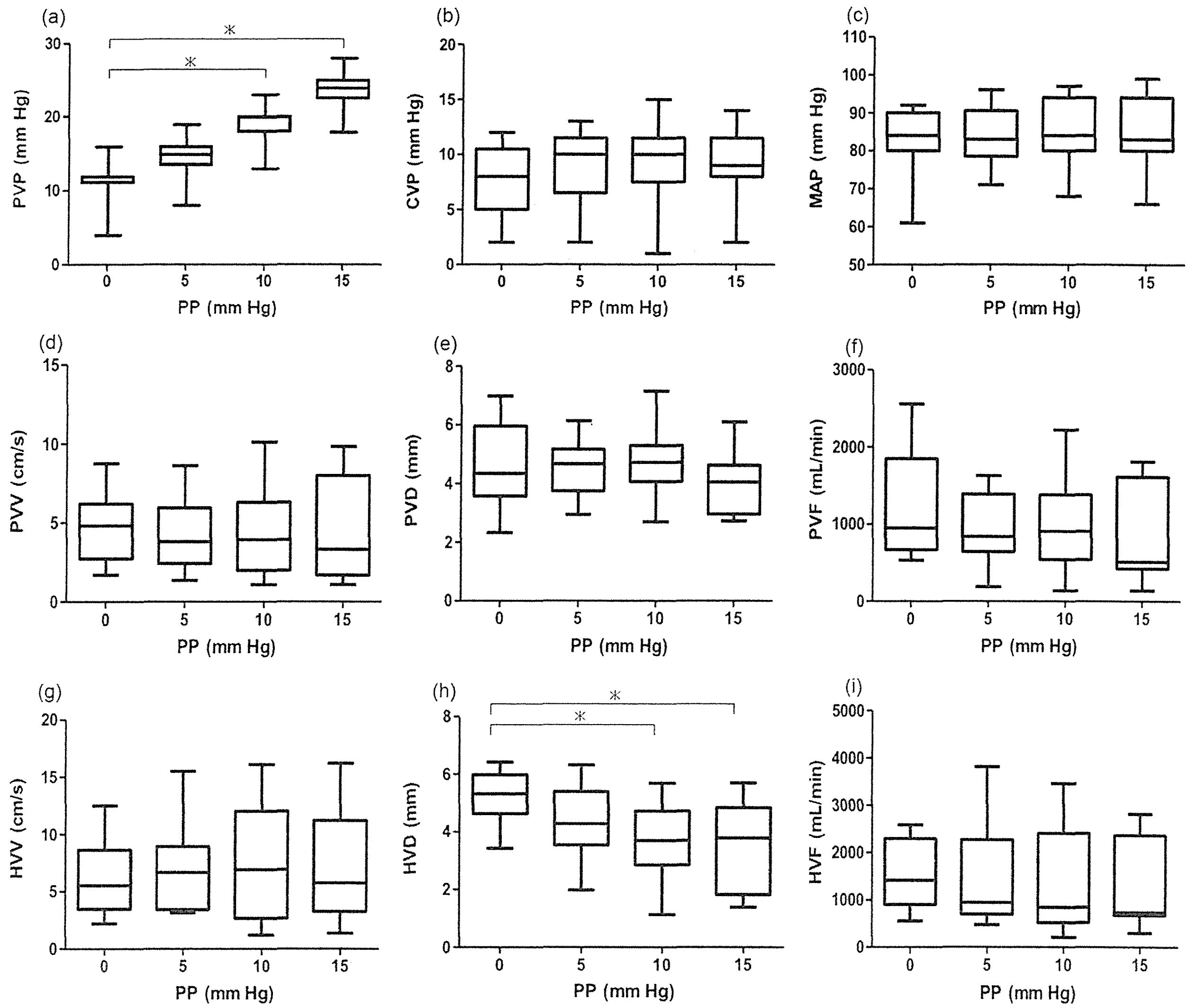

Fig. 3 Box plots showing (**a**) portal venous pressure (PVP), (**b**) central venous pressure (CVP), (**c**) mean arterial pressure (MAP), (**d**) portal venous velocity (PVV), (**e**) portal venous diameter (PVD), (**f**) portal venous flow (PVF), (**g**) hepatic venous velocity (HVV), (**h**) hepatic 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, $paCO_2$, HR, and end-tidal CO_2 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_2, tachycardia of 150–230 beats/min, increased end-tidal CO_2 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

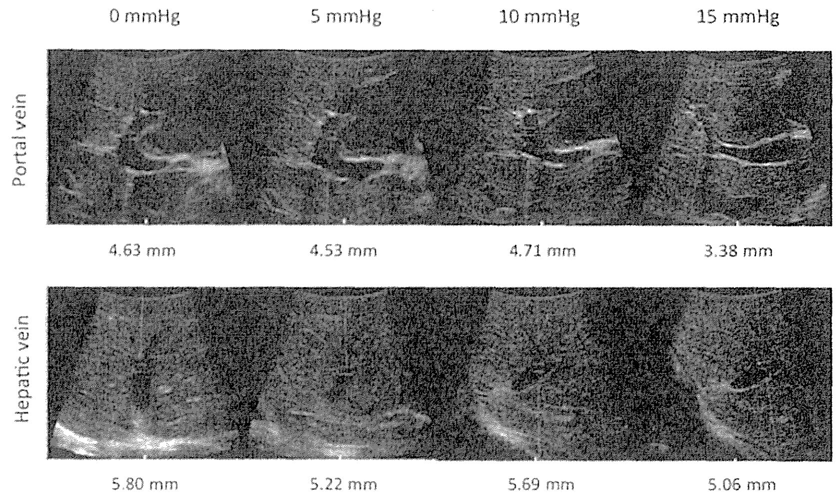

Fig. 4 Morphological changes of portal vein and hepatic vein diameter by ultrasonography

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)[a]	40 min[b]	*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_2 (mmHg)	408 (310–510)	293.5 (99–510)	0.02
$paCO_2$ (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_2 (mmHg)	43.50 (28–60)	57.50 (34–68)	0.02

[a] The time after which PP changed from 15 mmHg to 20 mmHg after LH was set as the baseline (0 min)

[b] PP was 20 mmHg

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_2 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 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 pO_2 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.

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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

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Abstract

Liver metastases resulting from primary choroidal malignant melanomas occur frequently and have a poor prognosis. As a result of advancements in multidisciplinary 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

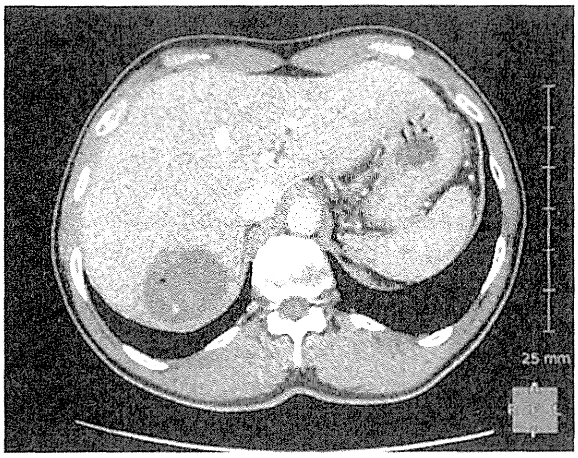

Figure 1 Preoperative abdominal CT. The metastatic melanoma was located in S7. *There were no other tumors in the liver or other organs.*

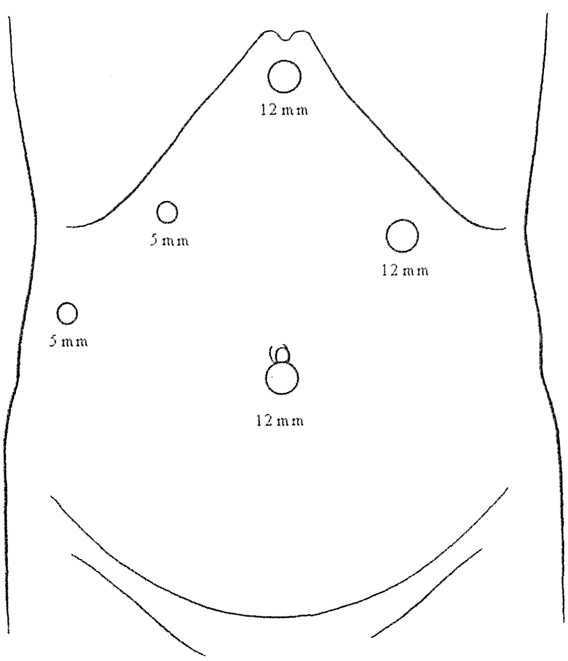

Figure 2 Port placements for pure laparoscopic posterior sectionectomy. The patient was placed in the left semilateral position. Three 12-mm ports and two 5-mm ports were used.

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

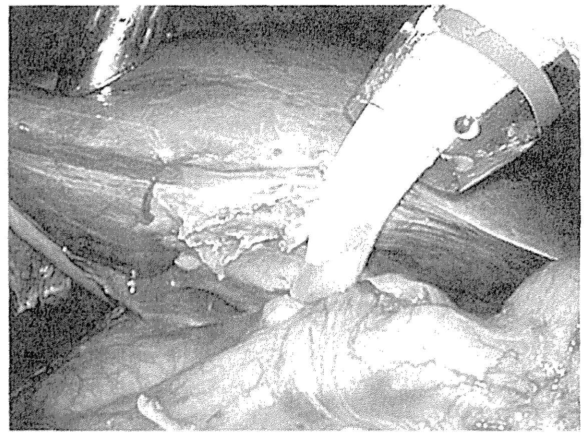

Figure 3 Laparoscopic Pringle's method before hepatic parenchymal transection. A vessel tape was passed around the hepatoduodenal ligament and tied through a soft catheter.

Figure 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.