Impact of obstructive ventilatory impairment on intraoperative bleeding during laparoscopic hepatectomy

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Abstract

Purpose:

An animal model of laparoscopic hepatectomy showed that bleeding from the hepatic vein is influenced by airway pressure. However, there are little research reports on how airway pressure leads to risks in clinical practice. The main objective of this study was to investigate the impact of preoperative forced expiratory volume % in 1 second (FEV1.0%) on intraoperative blood loss in laparoscopic hepatectomy.

Methods:

All patients who underwent pure laparoscopic or open hepatectomy from April 2011 to July 2020 were classified into two groups by preoperative spirometry: those with obstructive ventilatory impairment (Obstructive group; FEV1.0%< 70%) and those with normal respiratory function (Normal group; FEV1.0%≥ 70%). Massive blood loss was defined as 400 mL for laparoscopic hepatectomy.

Results:

In total, 247 and 445 patients underwent pure laparoscopic and open hepatectomy, respectively. Regarding laparoscopic hepatectomy group, blood loss was significantly greater in the Obstructive group (122 vs. 100 mL, $P = 0.042$). Multivariate analysis revealed that high IWATE criteria scores (≥ 7, odds ratio [OR]: 4.50, $P = 0.004$) and low preoperative FEV1.0% (< 70%, OR: 2.28, $P = 0.043$) were independent risk factors for blood loss during laparoscopic hepatectomy. In contrast, FEV1.0% did not affect the blood loss (522 vs. 605 mL, $P = 0.113$) during open hepatectomy.

Conclusion:

Obstructive ventilatory impairment (low FEV1.0%) may affect the amount of bleeding during laparoscopic hepatectomy.

Introduction

Laparoscopic hepatectomy has been increasingly performed in recent years. The advantages of laparoscopic hepatectomy are the magnification provided by the laparoscope and suppression of bleeding from the hepatic vein during liver dissection by the pneumoperitoneal pressure [1]. However, the control of intraoperative bleeding remains problematic [2]. In patients undergoing hepatectomy, massive intraoperative blood loss is correlated with postoperative morbidity, mortality, and long-term outcomes [3-8]. Thus, a problem of particular interest for liver surgeons is control of bleeding during hepatectomy. Such bleeding is caused by two factors: inflow from the hepatic artery and portal vein and outflow from the hepatic vein. The Pringle maneuver is reportedly effective in controlling bleeding from inflow, whereas bleeding from outflow is influenced by the central venous pressure (CVP) [9-11].

Notably, the animal study has suggested that airway pressure (AWP) influences CVP during laparoscopic hepatectomy [12]. However, there is little research reports on how AWP leads to risks in real clinical practice. If the AWP is measured directly, there are several difficulties since AWP varies with respiration. Moreover, the problems include at which point AWP should be measured, or whether the AWP value should be the highest, lowest, or average value. In the previous animal experiment, each parameter was measured in a setting that artificially kept the AWP constant, with no mention of respiratory variation in AWP [12]. In contrast, such invasive measurements cannot be performed on humans, thus making it difficult to collect data which may be one of the reasons for the lack of research reports.

Therefore, we focused on forced expiratory volume % in 1 second (FEV1.0%) because obstructive ventilatory impairment related to airway resistance is one of the causes of increased AWP and it is easy to measure by spirometry, which is routinely performed as a preoperative screening test [13-15]. The main purpose of this study was to investigate the impact of FEV1.0% measured by spirometry preoperatively on intraoperative blood loss during laparoscopic hepatectomy.

Materials And Methods

Patient selection and study design

We performed laparoscopic or open hepatectomy for 1058 patients with hepatocellular carcinoma or metastatic liver cancer in our department from April 2011 to July 2020. Of these patients, we excluded 366 patients who had a history of previous hepatectomy or upper abdominal surgery other than laparoscopic cholecystectomy, required simultaneous resection of other organs, cases of preoperative percutaneous transhepatic portal vein embolization that were not performed laparoscopically, and had not undergone preoperative spirometry. Thus, the present study finally included 692 patients (Figure 1).

Eleven patients required conversion to laparotomy. One of these patients required conversion because of uncontrollable bleeding from major hepatic veins that had been difficult to stop with laparoscopic manipulation and was allocated to the laparoscopic hepatectomy group. The remaining 10 patients who required conversion to laparotomy for reasons other than bleeding were allocated to the open hepatectomy group. We retrospectively analyzed the medical records of 247 patients who underwent pure laparoscopic hepatectomy. To compare blood loss during laparoscopic hepatectomy with that during open hepatectomy, we also identified 445 patient who underwent open hepatectomy during the same period.

All patients in this study were classified into two groups based on their preoperative spirometry findings: those who had obstructive ventilatory impairment with a FEV1.0% of <70% (Obstructive group) and those who had normal respiratory function with a FEV1.0% of ≥70% (Normal group) [13-15].

This study was approved by the Institutional Review Board of Shizuoka Cancer Center (approval number: J2020-75). Patient consent for participation was obtained using the opt-out method.

Surgical procedure of hepatectomy

Each patient's surgical procedure and extent of hepatectomy were determined by a weekly hepato-biliary-pancreatic cancer board and department meeting. We classified the type of hepatectomy according to the Brisbane 2000 terminology as partial resection, left lateral sectionectomy, segmentectomy, sectionectomy, and hemi-hepatectomy [16]. Although we began to perform laparoscopic hepatectomy in April 2011, procedures such as hemi-hepatectomy, sectionectomy (excluding left lateral sectionectomy), and segmentectomy were performed by laparotomy until December 2017. In the present study, we defined hemi-hepatectomy and sectionectomy (excluding left lateral sectionectomy) as major hepatectomy. We used the IWATE criteria to assess the difficulty of the laparoscopic procedures [17]. In this scoring system, a score of ≥7 points was recognized as extremely difficult. Because procedures involving more than sectionectomy are generally assigned a score of ≥7 points, we classified more than sectionectomy as major hepatectomy.

In both laparoscopic and open hepatectomy, liver dissection was performed using the clamp-crush technique, an ultrasonic coagulation incision device, and/or an ultrasonic surgical aspiration device. The hepatoduodenal mesentery was routinely taped, and the Pringle maneuver was performed using forceps or a tourniquet technique with a soft catheter if possible (15 min of clamping followed by 5 min of de-clamping) [2)]. The total blocking time was measured. The hepatic vessels were processed either individually or by the Glissonian pedicle approach [1].

The department of surgery requested the anesthesiology department to refrain from positive pressure ventilation and to limit the volume of ventilation and fluids infusion so that the CVP would not rise as much as possible. The anesthesia method for each case was decided at the anesthesiology meeting. The exact values for respiratory and circulatory control were adjusted intraoperatively by each anesthesiologist, generally in accordance with the requests.

During laparoscopic hepatectomy, the carbon dioxide pneumoperitoneal pressure was always set at 10 mmHg and the patient was placed head high during the procedure. One trocar was inserted under direct vision as a camera port with a balloon at or around the umbilicus. Four 5-mm and 12-mm trocars were inserted in the upper abdomen; the positions of the trocars were then adjusted for each procedure, and additional trocars were added as necessary. Laparotomy for open hepatectomy was performed through a midline or inverted L-shaped lateral abdominal incision.

Evaluation items

The main purpose of this study was to assess the correlation between preoperative FEV1.0% and blood loss during laparoscopic hepatectomy. We analyzed the patients' preoperative backgrounds, operative factors, tumor factors, and postoperative factors, which were graded according to the Clavien–Dindo classification. Respiratory complications were defined as respiratory failure with hypoxemia. We also evaluated the relationship between preoperative FEV1.0% and blood loss in patients who underwent open hepatectomy.

Statistical analysis

Continuous variables are expressed as median and interquartile range and were compared using the Mann–Whitney U test. Categorical variables were compared using the χ^2 test or Fisher's exact test, as appropriate. Binomial logistic regression was used for the univariate and multivariate analyses, and all factors found to be significant risk factors for massive blood loss during hepatectomy by the univariate analysis were entered into the multivariate analysis. We defined massive bleeding as four times the median blood loss of all laparoscopic or open hepatectomies.

All statistical analyses were performed using EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan), which is a graphical user interface for R (R Foundation for Statistical Computing, Vienna, Austria). More precisely, it is a modified version of R commander designed to add statistical functions frequently used in biostatistics. A *P*-value of <0.050 was considered statistically significant.

Results

Perioperative characteristics of patients undergoing laparoscopic hepatectomy according to respiratory function

Among the 247 patients who underwent laparoscopic hepatectomy, 76 and 171 were classified into the Obstructive and Normal groups, respectively. Table 1 shows the perioperative characteristics of the patients who underwent laparoscopic hepatectomy. Age and the number of male patients were significantly greater in the Obstructive group than Normal group. In the Obstructive group, only 7.9% of patients were diagnosed with chronic obstructive pulmonary disease (COPD). Although the patients in the Obstructive group had significantly better coagulation function in terms of the prothrombin percentage activity (104% vs. 98%, *P* = 0.045), blood loss was significantly greater in the Obstructive group (122 vs. 100 mL, *P* = 0.042) along with the operation time (238 vs. 198 min, *P* = 0.036). No significant differences in postoperative complications were found between the two groups (17.1% vs. 9.9%, *P* = 0.179).

The median blood loss during laparoscopic hepatectomy was 100 mL, and 400 mL, almost the top 10% value (11.7%), was defined as the cut-off value for massive bleeding during laparoscopic hepatectomy. The number of patients with massive blood loss during laparoscopic hepatectomy was 29. The multivariate analysis revealed that high IWATE criteria scores (≥7 points, odds ratio [OR]: 4.50, 95% confidence interval [CI]: 1.61–12.5, *P* = 0.004) and low preoperative FEV1% (<70 %, OR: 2.28, 95% CI: 1.02–5.10, *P* = 0.043) were independent risk factors for massive blood loss during laparoscopic hepatectomy (Table 2).

Perioperative characteristics of patients undergoing open hepatectomy according to respiratory function

We compared the perioperative characteristics between the Obstructive and Normal groups of patients who underwent open hepatectomy in a similar way to the corresponding comparisons for laparoscopic hepatectomy (Table 3). In contrast to laparoscopic hepatectomy, we found no significant difference in blood loss between the Obstructive and Normal groups (522 vs. 605 mL, $P = 0.113$) during open hepatectomy. Since the cutoff value for multivariate analysis was set at almost the top 10% tile in laparoscopic hepatectomy, that was also set at 1700 mL which was almost the top 10% tile in the open hepatectomy. The number of patients with massive blood loss during open hepatectomy was 47 (10.6%). The multivariate analysis showed that the body mass index (≥ 30 kg/m^2, OR: 7.43, 95% CI: 2.26–24.4, $P < 0.001$), indocyanine green clearance rate (ICG-K< 0.15 g/dL, OR: 3.07, 95% CI: 1.59–5.89, $P < 0.001$) and major hepatectomy (sectionectomy and hemi-hepatectomy, OR: 2.28, 95% CI: 1.12–4.66, $P = 0.023$) were independent risk factors for massive blood loss (≥ 1700 mL) during open hepatectomy (Table 4). Preoperative FEV1.0% was not an independent risk factor for intraoperative blood loss during open hepatectomy (OR: 1.06, 95% CI: 0.23–4.77, $P = 0.938$).

Discussion

The findings of the present study suggest that the amount of blood loss is greater in patients with obstructive ventilatory impairment than in those with normal respiratory function undergoing laparoscopic hepatectomy, whereas obstructive ventilatory impairment has no impact on the amount of blood loss during open hepatectomy. To our knowledge, this is the first study to demonstrate the relationship between FEV1.0% and blood loss during laparoscopic hepatectomy in actual clinical practice; this topic has only been previously investigated in an experimental animal study [12]. One advantage of the present study is that we assessed preoperative risk based on spirometry findings, which are simple to obtain and commonly determined in clinical practice. During hepatic dissection, if the hepatic venous pressure is high, bleeding will increase even by the minute hepatic vein injury. Under conditions of poor visual field, attempting to stop bleeding often results in further tearing of the hepatic veins and a rapid increase in bleeding. Even if hemostasis is achieved, manipulation under poor visual field may lead to Glisson injury, resulting in postoperative bile leak, which is still a common postoperative complication. In the present study, the median difference in blood loss between Obstructive group and Normal group in laparoscopic hepatectomy was slightly 22 mL, which seems rather small but has statistical significance because laparoscopic hepatectomy requires less blood loss by nature. However, liver surgeons are aware of the fear that small bleeding can lead to serious complications especially during laparoscopic hepatectomy, so it is extremely important to understand this as a preoperative risk.

The current study revealed two risk factors for massive blood loss during laparoscopic hepatectomy. One of these risk factors was low preoperative FEV1.0%. Previous studies have shown that low FEV1.0% is found in patients with COPD and/or obstructive ventilatory impairment and that AWP tends to be higher in such patients [14,15,18-20]. In the present study, the number of COPD patients in the Obstructive group was very low, only 6 (7.9%). This is reasonable because previous studies have shown that there is a discrepancy between the number of potential COPD patients and the number of patients who are actually diagnosed with COPD and receive respiratory rehabilitation and drug therapy [14]. In this study, COPD patients may have been the most appropriate subjects for evaluation, but the sample size was so small that it was difficult to evaluate the study items using only these cases. Thus, we thought it would be desirable to obtain the actual spirometry measurements. As a countermeasure for patients with obstructive ventilatory impairment, preoperative respiratory rehabilitation or drug therapy was performed as is done for COPD patients in our study; however, re-measurement of spirometry was not performed after the intervention. Therefore, it could not be assessed to what extent the preoperative respiratory rehabilitation and pharmacotherapy improved respiratory function, and the effect was unknown. Additional research is needed determine the effectiveness of preoperative respiratory rehabilitation and pharmacotherapy in reducing intraoperative blood loss.

CVP is related to the amount of blood loss, and several methods for reducing CVP have thus been reported (e.g., positioning, fluid restriction, and inferior vena cava semi-clamping) [21-23]. During open hepatectomy, decreasing ventilation alone does not reduce bleeding from outflow, whereas setting the positive end-expiratory pressure to zero and decreasing ventilation reportedly reduces intraoperative blood loss [24, 25]. In an animal model, increases in pneumoperitoneal pressure led to increases in CVP under high-AWP conditions during laparoscopic hepatectomy [12]. Thus, some researchers have suggested that in critical hemostatic situations during laparoscopic hepatectomy, lowering the CVP by lowering the AWP by 5 cm H_2O should be the first intervention implemented; reducing the AWP to minimal levels by short periods of no ventilation is another reported option [2, 12, 26]. However, intraoperative respiratory acidosis and postoperative respiratory complications may occur more frequently if these measures are performed excessively. Currently, no data clearly indicate how best to reduce the AWP during laparoscopic hepatectomy. How to optimally change the AWP in accordance with the degree of obstructive ventilatory impairment requires further evaluation.

A system for scoring the difficulty of laparoscopic hepatectomy (which was another risk factor for massive blood loss during laparoscopic hepatectomy in the current study) was proposed in 2014, and subsequent studies confirmed this system's validity and usefulness [27]. However, this scoring system has some limitations and is therefore best combined with the four levels of difficulty of the IWATE criteria, which are significantly correlated with the operative time, blood loss, and complication rates [17, 28]. Surgery on patients with scores of ≥7 by the IWATE criteria has been classified as more difficult, and these patients reportedly differ significantly in intraoperative blood loss and operative time compared with patients who have scores of <7 [28]. In our multivariate analysis, the OR of the IWATE criteria was higher than that of low FEV1.0%, suggesting that surgical difficulty may have an even greater impact on massive bleeding than respiratory function. In very difficult cases in daily clinical practice, patients with IWATE criteria scores of ≥7 who also have obstructive ventilatory impairment are candidates for hepatectomy, and the benefit of a laparoscopic approach should be carefully balanced against the increased risk of bleeding.

This study had some limitations. The first is its retrospective design and single-center setting. Although our sample size was not small, sample sizes differed between the laparoscopic and open hepatectomy groups. Further prospective multicenter studies are needed to validate our findings with matched patient background and sample size. Second, we could not assess fluctuations in intraoperative AWP and hemodynamics because intraoperative respiratory control and CVP were not recorded. Even if these records are to be obtained, the method of their measurement needs to be discussed in detail and the environment needs to be designed. In addition, although we requested the anesthesiology department to maintain a low CVP for intraoperative respiratory management, the actual adjustment was different in each case, so it was difficult to exactly match the conditions. In order to solve these problems, prospective multicenter studies are likely to be necessary. Third, this study did not include patients with diseases such as intrahepatic cholangiocarcinoma and benign tumors; only patients with hepatocellular carcinoma and metastatic liver cancer were included. Therefore, other types of diseases need to be studied.

Conclusion

We found that obstructive ventilatory impairment may affect bleeding during laparoscopic hepatectomy. It is hoped that future studies will be advanced to examine the reduction of blood loss by paying attention to respiratory management in perioperative management.

Declarations

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Author contribution

Study conception and design: MN, YO

Acquisition of data: MN, YO, TS, RA, KO, MY, SO, and KU

Analysis and interpretation of data: MN, YO, YK

Drafting of manuscript: MN, YO

Critical revision of manuscript: All authors

Conflicts of interest

None of the authors have personal conflicts of interest associated with the publication of this article.

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Tables

Table 1 Perioperative characteristics of patients in laparoscopic hepatectomy.

	Obstructive group	Normal group	*P*
	n=76	n=171	
Age, years #	70 (37-90)	68 (24-89)	***0.008***
Gender (male), No. (%)	65 (85.5)	113 (66.0)	***0.001***
Body mass index, kg m^{2}#	23.4 (17.7-32.0)	22.9 (10.0-33.6)	0.554
Medical history			
Preoperative chemotherapy, No. (%)	4 (5.3)	6 (3.5)	0.502
Antithrombotic agent medication, No. (%)	1 (1.3)	8 (4.6)	0.282
COPD, No. (%)	6 (7.9)	0 (0.0)	***< 0.001***
Smoker, No. (%)	11 (14.5)	18 (10.5)	0.395
Liver function			
Albumin, g/dL#	4.3 (3.4-5.0)	4.3 (2.8-7.3)	0.674
Prothrombin time, %#	104 (51-131)	98 (60-129)	***0.045***
Total bilirubin, mg/dL#	0.6 (0.3-1.7)	0.6 (0.2-2.0)	0.709
Platelets, $\times 10^{4}/\mu L$#	20.1 (9.1-35.2)	19.0 (6.2-42.7)	0.096
ICG-R15, %#	8.5 (0.7-29.0)	7.3 (1.4-44.5)	0.201
ICG-K#	0.17 (0.08-0.33)	0.18 (0.05-0.34)	0.127
Characteristics of surgery			
Operation time, min#	238 (58-496)	198 (49-678)	***0.036***
Pringle maneuver time, min#	53 (0-240)	72 (0-240)	0.535
Blood loss, ml#	122 (0-1089)	100 (0-8923)	***0.042***
Intraoperative total fluid input, mL#	1850 (500-3750)	1700 (700-6050)	0.232
Intraoperative RBC transfusion, No. (%)	0 (0.0)	2 (1.1)	1.000
IWATE criteria, point#	5 (1-11)	4 (1-11)	0.087
Major hepatectomy, No. (%)	8 (10.5)	10 (5.8)	0.195
Type of surgery procedure			0.505
Partial resection, No. (%)	57 (75.0)	126 (73.7)	

Left lateral sectionectomy, No. (%)	8 (10.5)	28 (16.4)	
Segmentectomy, No. (%)	3 (3.9)	7 (4.1)	
Sectionectomy, No. (%)	3 (3.9)	5 (2.9)	
Hemi-hepatectomy, No. (%)	5 (6.6)	5 (2.9)	
Resected specimen			
Tumor size, mm#	27 (0-62)	23 (0-122)	0.288
Number, No. #	1 (1-4)	1 (1-5)	0.258
Postoperative complications, No. (%)	13 (17.1)	17 (9.9)	0.139
Bile leak, No. (%)	1 (1.3)	2 (1.2)	1.000
Abscess, No. (%)	2 (2.6)	4 (2.3)	1.000
Wound infection, No. (%)	2 (2.6)	3 (1.8)	0.645
Respiratory complication, No. (%)	1 (1.3)	1 (0.6)	0.522

Obstructive group: Obstructive ventilation disorder group, Normal group: Normal respiratory function group, COPD: chronic obstructive pulmonary disease, RBC: red blood cell, ICG-R15: Indocyanine green retention rate at 15 minutes, ICG-K: Indocyanine green clearance rate.

Major hepatectomy; sectionectomy (except left lateral sectionectomy), hemi-hepatectomy.

Respiratory complication respiratory failure with hypoxemia such as pneumonia or atelectasis.

Values in parentheses are percentages unless otherwise indicated.

Values are shown as the #median (range).

Table 2 Preoperative predictors for massive bleeding (≥ 400ml) in laparoscopic hepatectomy

Variables (N=247)	No.	%	Univariate		Multivariate	
			Odds ratio (95% Confidence interval)	*P*	Odds ratio (95% Confidence interval)	*P*
Age (≥ 80 years)	23	9.3	0.31 (0.04-2.45)	0.272		
Gender (males)	178	72.0	1.99 (0.72-5.46)	0.179		
Body mass index (≥30 kg/m^2)	12	4.8	0.67 (0.08-5.40)	0.709		
Preoperative chemotherapy	10	4.0	1.94 (0.39-9.64)	0.415		
Preoperative FEV1.0% (< 70%)	76	30.7	2.35 (1.07-5.15)	***0.033***	2.28 (1.02-5.10)	***0.043***
Antithrombotic agent medication	9	3.6	2.23 (0.44-11.3)	0.332		
Albumin (< 4.0 g/dL)	53	21.4	0.95 (0.36-2.47)	0.915		
Total bilirubin (> 1.2 mg/dL)	17	6.8	1.68 (0.45-6.24)	0.438		
Platelets (< 10×10^4/μL)	17	6.8	1.00 (0.21-4.63)	0.997		
Prothrombin time (< 70 %)	5	2.0	1.91 (0.20-17.7)	0.569		
ICG-R15 (≥ 10%)	83	33.6	1.05 (0.46-2.36)	0.915		
ICG-K (< 0.15)	57	23.0	1.07 (0.43-2.65)	0.885		
IWATE criteria (≥ 7)	21	8.5	4.64 (1.69-12.7)	***0.002***	4.50 (1.61-12.5)	***0.004***
Resected specimen number (≥ 2)	58	23.4	1.55 (0.66-3.63)	0.310		
FEV1.0%: Forced expiratory volume % in one second, ICG-R15: Indocyanine green retention rate at 15 minutes, ICG-K: Indocyanine green clearance rate.						

Table 3 Perioperative characteristics of patients in open hepatectomy

	Obstructive group	Normal group	*P*
	n=100	n=345	
Age, years #	70 (52-87)	67 (13-90)	***0.003***
Gender (males), No. (%)	83 (83.0)	246 (71.3)	***0.019***
Body mass index (kg/m^2) #	22.6 (16.3-33.5)	22.7 (15.1-37.2)	0.665
Medical history			
Preoperative chemotherapy, No. (%)	1 (1.0)	17 (4.9)	0.089
Antithrombotic agent medication, No. (%)	1 (1.0)	9 (2.6)	0.469
COPD, No. (%)	5 (5.0)	3 (0.9)	***0.016***
Smoker, No. (%)	16 (16.0)	55 (15.9)	1.000
Liver function			
Albumin, g/dL#	4.2 (3.0-5.6)	4.3 (2.6-5.1)	0.233
Prothrombin percentage activity, %#	93 (59.0-120)	96 (34.0-128)	0.051
Total bilirubin, mg/dL#	0.6 (0.2-1.3)	0.6 (0.2-2.6)	0.360
Platelets, $\times 10^4/\mu L$#	19.4 (6.8-64.4)	18.1 (5.5-47.7)	0.102
ICG-R15, %#	11.0 (0.7-33.0)	10.1 (1.0-65.0)	0.219
ICG-K#	0.16 (0.09-0.32)	0.16 (0.01-0.32)	0.440
Characteristics of surgery			
Operation time, min#	316 (90-3320)	326 (71-1012)	0.476
Blood loss, ml#	522 (34-5226)	605 (5-8499)	0.113
Intraoperative total fluid input, mL#	2900 (1180-10500)	3150 (950-31150)	***0.047***
Intraoperative RBC transfusion, No. (%)	10 (10.0)	29 (8.4)	0.688
Major hepatectomy, No. (%)	55 (55.0)	183 (53.0)	0.820
Type of surgery procedure			0.646
Partial resection, No. (%)	33 (33.0)	106 (30.7)	
Left lateral sectionectomy, No. (%)	5 (5.0)	13 (3.8)	
Segmentectomy, No. (%)	8 (8.0)	44 (12.8)	

Sectionectomy, No. (%)	31 (31.0)	95 (27.5)	
Hemi-hepatectomy, No. (%)	23 (23.0)	87 (25.2)	
Resected specimen			
Tumor size, mm#	30 (4-170)	32 (0-160)	0.491
Number, No. #	1 (1-10)	1 (1-10)	0.856
Postoperative complications, No. (%)	35 (35.0)	115 (33.3)	0.810
Bile leak, No. (%)	12 (12.0)	44 (12.8)	1.000
Abscess, No. (%)	0 (0.0)	8 (2.3)	0.208
Wound infection, No. (%)	9 (9.0)	32 (12.8)	1.000
Respiratory complication, No. (%)	6 (6.0)	27 (7.8)	0.667

Obstructive group: Obstructive ventilation disorder group, Normal group: Normal respiratory function group, COPD: chronic obstructive pulmonary disease, RBC: red blood cell, ICG-R15: Indocyanine green retention rate at 15 minutes, ICG-K: Indocyanine green clearance rate.

Major hepatectomy; sectionectomy (except left lateral sectionectomy), hemi-hepatectomy.

Respiratory complication respiratory failure with hypoxemia such as pneumonia or atelectasis.

Values in parentheses are percentages unless otherwise indicated.

Values are shown as the #median (range).

Table 4 Preoperative predictors for massive bleeding (≥ 1700 ml) in open hepatectomy

Variables (N=445)	No.	%	Univariate		Multivariate	
			Odds ratio (95% Confidence interval)	P	Odds ratio (95% Confidence interval)	P
Age (≥ 80 years)	40	9.0	0.66 (0.19-2.25)	0.512		
Gender (males)	329	73.9	2.16 (0.93-4.96)	0.070		
Body mass index (≥ 30 kg/m^2)	13	2.9	8.17 (2.62-25.5)	***< 0.001***	7.43 (2.26-24.4)	***< 0.001***
Preoperative chemotherapy	18	4.0	1.06 (0.23-4.77)	0.938		
Preoperative FEV1.0% (< 70%)	100	22.5	1.06 (0.51-2.17)	0.871		
Antithrombotic agent medication	10	2.2	0.94 (0.11-7.58)	0.953		
Albumin (< 4.0 g/dL)	74	16.6	1.86 (0.91-3.78)	0.087		
Total bilirubin (> 1.2 mg/dL)	25	5.6	1.67 (0.54-5.09)	0.367		
Platelets (< 10×10^4/μL)	11	2.5	1.92 (0.40-9.17)	0.413		
Prothrombin time (< 70 %)	15	3.4	1.32 (0.28-6.02)	0.723		
ICG-R15 (≥ 10%)	241	54.2	1.57 (0.84-2.94)	0.156		
ICG-K (< 0.15)	158	35.5	2.49 (1.35-4.60)	***0.003***	3.07 (1.59-5.89)	***< 0.001***
Major hepatectomy*	238	53.5	2.22 (1.15-4.27)	***0.017***	2.28 (1.12-4.66)	***0.023***
Tumor size (≥ 30 mm)	251	56.4	2.18 (1.12-4.26)	***0.022***	1.94 (0.95-3.96)	0.068
Resected specimen number (≥ 2)	140	31.5	0.91 (0.47-1.77)	0.794		

FEV1.0%: Forced expiratory volume % in one second, ICG-R15: Indocyanine green retention rate at 15 minutes, ICG-K: Indocyanine green clearance rate, Major hepatectomy; sectionectomy (except left lateral sectionectomy), hemi-hepatectomy.

Figures

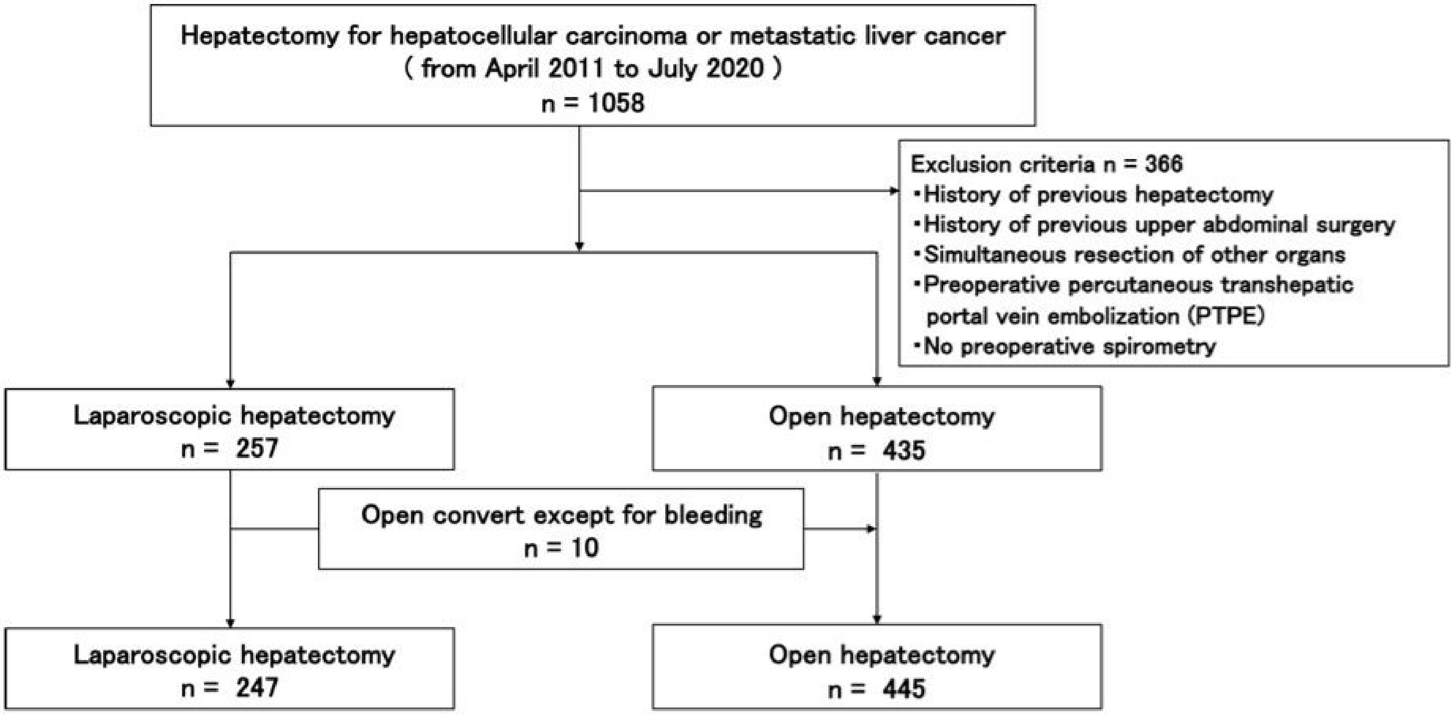

Figure 1

Patient flowchart of this study.