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Research Article

Impact of Intraoperative Gravity-Dependent Atelectasis Following Laparo scopic Liver Resection Performed in the Lateral Position

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Abstract

Laparoscopic liver resection (LLR) is currently an acceptable approach to liver surgery in select patients. The correlation between the intraoperative position and the presence of gravity-dependent atelectasis (GDA) has been well discussed. However, LLR is performed in the left half lateral position, and the relationship between this position and the presence of GDA remains unclear. We evaluated the extent to which the intraoperative left half lateral position affects the presence of GDA. Furthermore, univariate and multivariate analyses were performed to identify potential risk factors for postoperative complications after LLR with a special emphasis on the presence of GDA by comparing various patient-, liver- and surgery-related factors in a retrospective cohort. We retrospectively evaluated 129 patients who underwent LLR in the left half lateral position at the Saitama Cancer Center in Saitama, Japan, between March 2011 and July 2020. The frequency and duration of GDA were investigated. We divided the cohort into groups with GDA and without GDA based on a cutoff value ($\geq$ 5 days, n = 61 and < 5 days, n = 68, respectively). Using multivariate analysis, the duration of GDA and several risk factors for postoperative complications after LLR were independently assessed. Postoperative GDA was observed in 61 patients (47%) and lasted for 1 to 8 days in these patients. The mean duration of GDA was 4.3 days. Multivariate logistic regression analysis revealed that a GDA duration of 5 days or more (odds ratio [OR], 2.03; $p = 0.001$) and an operating time > 388 minutes (OR, 5.31; $p < 0.001$) were independent risk factors for postoperative complications after LLR. The incidence and duration of postoperative GDA are considered useful predictors of postoperative complications, and these predictors should be assessed to improve the short-term outcomes of patients undergoing LLR.

Introduction

Reich et al. initially reported the use of laparoscopic liver resection (LLR) for benign tumors in 1991, however the procedure is now used to treat primary and metastatic malignant tumors [1-3]. Initially, laparoscopic procedures were not widely accepted due to the difficulty in controlling bleeding. Improvements in laparoscopic techniques and instruments, as well as accumulated experience, have led to a wider acceptance of LLR by trained surgeons [4,5]. The international position on LLR was addressed by experts in hepatobiliary surgery at an international consensus conference in Louisville, Kentucky (USA) in November 2008 [6]. These experts concluded that LLR is considered a safe and effective approach when performed by experienced surgeons. Recent studies have suggested that LLR leads to fewer postoperative

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complications, such as operative blood loss, and a shorter duration of hospital stay than conventional open liver surgery [3,7-9]. Simillis et al. reported that the volume of operative blood loss and duration of hospital stay were significantly reduced after laparoscopic surgery [3]. Lesurtel et al. also reported that the laparoscopic approach was associated with less blood loss and the absence of specific postoperative complications of hepatic resection [10]. Regarding these complications, the relationship between postoperative thoracic complications and laparoscopic surgery has been well discussed. Previous studies have reported that thoracic complications are associated with longer operative times, an increased number of operative ports, larger values of positive end-tidal CO_2, and intraoperative positions [11,12]. In terms of thoracic complications and the intraoperative position, Craig et al initially reported that 30% of patients who underwent thoracic surgery in the lateral position exhibited gravity-dependent atelectasis (GDA) in the contralateral lung [13]. Zhao et al. also reported that 47% of patients who underwent laparoscopic urological surgery in the lateral position exhibited GDA in the contralateral lung [11]. In terms of LLR, which is performed in the left half lateral position, the relationship between this intraoperative position and the presence of GDA remains unclear. In this study, we evaluated the extent to which the intraoperative left half lateral position affects the presence of GDA. Furthermore, using univariate and multivariate analyses, we determined how the presence of GDA predicts postoperative complications by comparing various patient-, liver- and surgery-related factors in a retrospective cohort.

Materials and Methods

Patients

We retrospectively evaluated 217 consecutive patients who underwent LLR at the Saitama Cancer Center in Saitama, Japan, between March 2011 and July 2020. The ethics committee of the Saitama Cancer Center approved this study (#1115). First, we excluded 21 patients who underwent surgeries that were more extensive standard LLR procedures, such as simultaneous colectomy. Second, 67 patients who underwent LLR in the supine position were excluded. A total of 129 patients who underwent LLR in the left half lateral position were included in the final cohort.

Definition of the presence of GDA

We routinely performed postoperative plain chest radiography immediately after the operation and on postoperative days 1, 2, 3, 5 and 7. The presence of GDA was defined as evidence of atelectasis or infiltration in the left lung on plain chest radiographs taken immediately after the operation with respect to preoperative radiographs (Figures 1A and 1B). Similarly, an improvement in GDA was also recorded when there was no evidence of atelectasis or infiltration in the left lung on the plain chest radiographs. The frequency and duration of GDA were investigated. For the 129 patients who underwent LLR in the left half lateral position, the following patient characteristics were compared between the patients with and without GDA: age, sex, body mass index (BMI), American Society of Anesthesiologists

Figure 1A: A preoperative plain chest radiograph is shown.

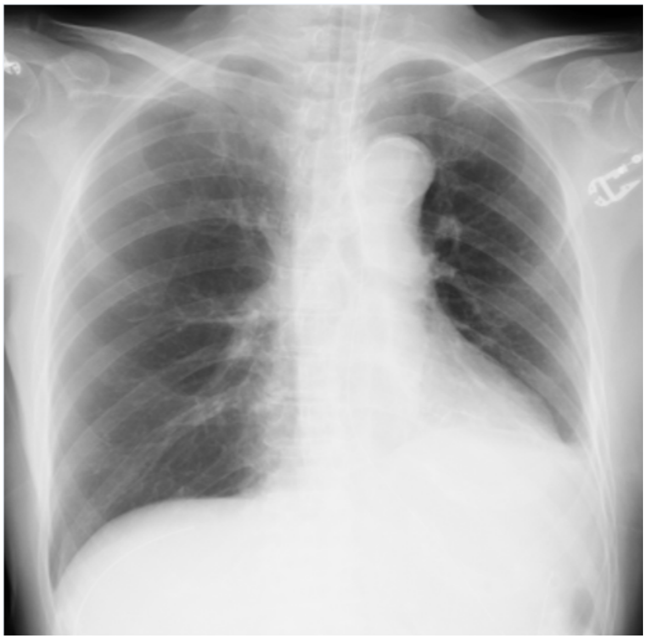

Figure 1B: A postoperative plain chest radiograph taken immediately after the operation is shown. This image shows an elevated diaphragm, with atelectasis or infiltration in the left lung, with respect to the preoperative findings. Therefore, this case was defined as positive for GDA.

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(ASA) score, history of respiratory comorbidities, history of diabetes mellitus, history of abdominal surgery, liver fibrosis, tumor size, number of lesions, tumor characteristics, surgical procedure, operating time, intraoperative blood loss volume, length of postoperative hospital stay and postoperative complications. Liver fibrosis was graded according to the Metavir scoring system [14]. Postoperative complications were also graded according to the Clavien–Dindo classification system [15].

Patient-, liver- and surgery-related risk factors for short-term outcomes

Univariate and multivariate analyses were performed to not only assess the duration of GDA but to also identify potential risk factors for postoperative complications after LLR by comparing various patient-, liver- and surgery-related factors. Cutoff values for each continuous variable were defined according to the ROC curve analysis results.

For patient-related risk factors, we focused on older age, male sex, high BMI, high ASA score, history of respiratory comorbidities, history of diabetes mellitus and history of abdominal surgery.

For liver-related factors, we collected data regarding tumor size (> 31 mm), multiple lesions, liver fibrosis (Metavir score F1 to F4) and malignant pathology.

For surgery-related factors, we focused on surgical procedure, operating time (> 388 minutes), and intraoperative blood loss (> 295 grams).

ROC curves visually represent the sensitivity (i.e., the probability of correctly identifying an event such as death) and specificity (i.e., the probability of correctly identifying a nonevent) of various cutoff values.

Surgical procedures and perioperative management

We routinely performed the laparoscopic technique with five ports, a 10-mmHg pneumoperitoneum and a flexible angle laparoscope. The hand-assisted technique was not used. Pringle's maneuver was routinely used [16]. Parenchymal liver transection was performed by the THUNDERBEAT™ system (TS) (Olympus Medical Systems Corp., Tokyo, Japan) and the Cavitron ultrasonic surgical aspirator (CUSA: Integra Lifesciences Corporation, NJ, USA). Bipolar coagulation was used to treat minor bleeding. The resected liver was placed in a plastic bag and extracted, without fragmentation, through a small abdominal incision. The drainage tube was routinely placed on the resected liver surface. The methods of managing the drain and checking the total bilirubin levels in the drainage fluid were standardized in this study. The drain was removed if the drainage fluid was clear and both bile leakage and bacterial contamination were absent. All patients received prophylactic antibiotics either intraoperatively or for 1 or 2 days postoperatively.

Statistical analyses

ROC curve analyses were used to evaluate and compare the sensitivity and specificity of the diagnostic tests and to identify cutoff values for continuous variables with positive test results for a certain outcome. The predictive ability of multiple models based on different factors was described using a concordance index, which is a measure of the predictive ability of a model and is equivalent to the area under the ROC curve. The concordance index ranges from 0.5 to 1.0; a value of 0.5 indicates no predictive ability and a value of 1.0 indicates perfect predictive ability. A model is considered reliable when the concordance index is greater than 0.8. Correlations with patient background data were analyzed using the χ^2 test or Fisher's exact test, as appropriate. For the multivariate analysis, a multiple logistic regression analysis that yields odds ratios and 95% confidence intervals (CIs) was used to identify risk factors for postoperative outcomes after LLR (with p values < 0.05). Statistical analyses were performed using a statistical analysis software package (SPSS Statistics, version 21; IBM, Armonk, NY, USA), and p values < 0.05 were considered significant.

Results

Patient characteristics

The backgrounds of the patients with or without GDA in the left half lateral position are presented in table 1. Significant differences were observed between the two groups with regard to BMI (p = 0.031), history of respiratory comorbidities (p = 0.001), history of diabetes mellitus (p < 0.001), operating time (p = 0.025), and postoperative complications (p = 0.001). The incidence of postoperative complications was greater than in the patients with GDA; there were 4 patients with mild-to-severe pneumonia, 2 patients with bile leakage and 1 patient with a surgical site infection. Similarly, among the patients without GDA, there was 1 patient with bile leakage and 1 patient with a surgical site infection.

Frequency and duration of GDA

In the present cohort, postoperative GDA was observed in 61 patients (47%). In these 61 patients, the duration of GDA ranged from 1 to 8 days. The values of the duration of GDA were normally distributed. The mean duration of GDA was 4.3 days. Therefore, 5 days was used as the cutoff value in the present study.

Univariate analyses of risk factors for short-term outcomes during different treatment phases (Table 2)

There was a significant difference in the duration with GDA with respect to the incidence of postoperative complications (high, 4 (44%) vs. low, 3 (5.7%), p < 0.001). Mild-to-severe pneumonia was observed in all 4 patients with GDA and lasted more than 5 days.

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Table 1: Patient characteristics

Factors	with GDA (n = 61)	without GDA (n = 68)	p value
Age	71 (46-90)	69 (30-87)	0.211
Sex ratio (male: female)	39: 22	39: 29	0.113
BMI (kg/m^2)	25.8 ± 3.15	22.5 ± 2.18	0.031*
ASA score (1-4)	2 (1-3)	2 (1-3)	0.855
History of respiratory comorbidity			
Yes	8 (13%)	1 (1.4%)	0.001*
No	53 (86%)	67 (98%)	
History of diabetes mellitus			
Yes	23 (38%)	4 (5.8%)	<0.001*
No	38 (62%)	64 (94%)	
History of abdominal surgery			
Yes	15 (24%)	14 (21%)	0.339
No	46 (76%)	54 (79%)	
Liver fibrosis (Metavir score)			
F0	46 (75%)	61 (89%)	0.331
F1-F3	11 (18%)	5 (7.3%)	
F4	4 (6.5%)	2 (2.9%)	
Tumor size (mm)	29.3 ± 11.5	32.5 ± 22.1	0.114
Number of leisions			
1	49 (80%)	56 (82%)	0.551
2	11 (18%)	10 (14%)	
3	1 (1.6%)	2 (2.9%)	
Tumor characteristics			
HCC	29 (47%)	24 (35%)	0.212
Cholangiocarcinoma	0	3 (4.4%)	
CRLM	26 (42%)	32 (47%)	
Other metastasis	1 (1.6%)	3 (4.4%)	
Others	5 (8.1%)	6 (8.8%)	
Surgical procedure			
Partial resection	46 (75%)	60 (88%)	0.075
Segmentectomy	6 (9.8%)	2 (2.9%)	
Sectionectomy	7 (11%)	5 (7.3%)	
Others	2 (3.2%)	1(1.4%)	
Operating time (minutes)	427 ± 225	315 ± 139	0.025*
Intraoperative blood loss volume (g)	313 ± 358	244 ± 319	0.441
Length of postoperative hospital stay (days)	7 (6-22)	7 (5-24)	0.116
Postoperative complications (C-D grade)			
None/I	54 (88%)	68 (100%)	0.001*
II/III/IV	7 (12%)	0	

Footnote: GDA, gravity dependent atelectasis; BMI, body mass index; ASA, American Society of Anesthesiologists; HCC, hepatocellular carcinoma; CRLM, colorectal liver metastases; C-D, Clavien-Dindo.
*: $p < 0.05$

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Table 2: Risk factors for short-term outcome

Parameter	Cut-off value	No. of Patients	None and C-D Grade I	C-D Grades II, III and IV	p value
Duration with GDA (days)					
High	5	9	5 (55%)	4 (44%)	< 0.001*
Low		52	49 (94%)	3 (5.7%)	
Age					
High	71	32	27 (84%)	5 (15%)	0.081
Low		29	27 (93%)	2 (6.8%)	
Sex					
Male		39	35 (89%)	4 (10%)	0.620
Female		22	19 (86%)	3 (14%)	
BMI (kg/m^2)					
High	25	31	26 (84%)	5 (16%)	0.045*
Low		30	28 (93%)	2 (6.6%)	
ASA score (1-4)					
High	2	35	30 (86%)	5 (14%)	0.260
Low		26	24 (92%)	2 (7.6%)	
History of respiratory comorbidity					
Yes		8	6 (75%)	2 (25%)	0.035*
No		53	48 (90%)	5 (10%)	
History of diabetes mellitus					
Yes		23	19 (82%)	4 (17%)	0.015*
No		38	35 (92%)	3 (7.8%)	
History of abdominal surgery					
Yes		15	13 (86%)	2 (13%)	0.131
No		46	41 (89%)	5 (10%)	
Tumor size (mm)					
High	31	32	27 (84%)	5 (15%)	0.081
Low		29	27 (93%)	2 (6.8%)	
Multiple lesions					
Yes		12	11 (91%)	1 (8.3%)	0.131
No		49	43 (88%)	6 (12%)	
Liver fibrosis (Metavir score)					
F0		46	41 (89%)	5 (10%)	0.211
F1-F4		15	13 (86%)	2 (13%)	
Malignant pathology					
Yes		56	50 (89%)	6 (10%)	0.065
No		5	4 (80%)	1 (20%)	
Extent of liver resection					
Partial resection		46	41 (89%)	5 (10%)	0.556
Others		15	13 (87%)	2 (13%)	
Operating time (minutes)					
High	388	31	25 (81%)	6 (19%)	0.001*
Low		30	29 (97%)	1 (3.3%)	
Intraoperative blood loss volume (grams)					
High	295	32	27 (84%)	5 (15%)	0.081
Low		29	27 (93%)	2 (6.8%)	

Footnotes: C-D, Clavien-Dindo; GDA, gravity dependent atelectasis; BMI, body mass index; ASA, American Society of Anesthesiology
*: $p < 0.05$

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In terms of the patient-related risk factors, BMI (high, 5 (15%) vs. low, 2 (6.8%), p = 0.045), a history of respiratory comorbidities (yes, 2 (25%) vs. no, 5 (10%), p = 0.035), and a history of diabetes mellitus (yes, 4 (17%) vs. no, 3 (7.8%), p = 0.015) significantly affected the incidence of postoperative complications.

No parameters significantly affected the incidence of postoperative complications with respect to liver-related risk factors.

In terms of surgery-related risk factors, operating time (> 388 minutes, 6 (19%) vs. < 388 minutes, 1 (3.3%), p = 0.001) significantly affected the incidence of postoperative complications. There were 4 patients with mild-to-severe pneumonia, 1 patient with bile leakage and 1 patient, within the group of patients with an operating time of more than 388 minutes, with a surgical site infection.

Multivariate analysis (Table 3)

For the multivariate analysis, the following prognostic factors were identified using a multiple logistic regression analysis: GDA duration of 5 days or more, BMI > 25 kg/m^2, history of respiratory comorbidities, history of diabetes mellitus, and operating time > 388 minutes. Multivariate logistic regression analysis revealed that a GDA duration of 5 days or more (odds ratio [OR], 2.03; p = 0.001) and an operating time > 388 minutes (OR, 5.31; p < 0.001) were independent risk factors for postoperative complications after LLR.

Discussion

In the present study, postoperative GDA was observed in 61 patients (47%), and the mean duration of GDA was 4.3 days (1-8 days). Furthermore, the multivariate analysis results indicated that the incidence of postoperative GDA correlated with the postoperative outcomes of the patients who underwent LLR in the left half lateral position. In fact, mild-to-severe pneumonia was observed in all 4 patients with GDA and lasted more than 5 days. Thus, the incidence and duration of postoperative GDA are assumed to be useful predictors for postoperative complications, and these predictors should be assessed to improve the short-term outcomes of patients undergoing LLR. In terms of the mechanism that causes GDA after surgery in the lateral position, Rheder et al was the first to suggest that there is a preferential distribution of tidal volume to the nondependent lung and preferential ventilation of the dependent lung in the lateral position [17]. Furthermore, it has also been reported that not only an increase in abdominal pressure by laparoscopic surgery but also relaxation of the diaphragm with the use of muscle relaxants elevate the diaphragm, which further decreases the functional residual capacity of the lower lungs [17]. Regarding the increase in abdominal pressure, it is suggested that the pneumoperitoneum pressure in laparoscopic surgery may further raise the diaphragm and cause ventilation disorders. Furthermore, Kaneko et al showed that in subjects in the lateral position with lung volumes of less than 50% of total lung capacity, the nondependent regions of the lung received a relatively large proportion of the inspired volume [18]. Long-term outcomes of LLR have been reported in some previous studies [7,19,20]. The results of these studies revealed that LLR was comparable to conventional open liver resection in terms of resection margins, recurrence rates, and long-term outcomes. However, the short-term outcomes of LLR have rarely been discussed until now. The reason for the lack of studies on short-term outcomes and risk factors for postoperative complications is that strict patient selection criteria for LLR were established by an international consensus on LLR [6]. Tranchart et al. first reported that the postoperative complication rate increases by 60% with each additional increment of time required for LLR [7]. The potential relationship between operating time and risk of short-term outcomes was initially reported in 1960 [21,22]. Nobili et al reported that operating time was identified by multivariate analysis as an independent risk factor for pulmonary and infectious complications after open hepatic resection [23]. According to our multivariate analysis, in addition to operating time, a GDA duration of 5 days was revealed to be an independent risk factor for postoperative complications after LLR. Questions regarding the mechanisms by which the incidence of postoperative GDA potentially affects the postoperative outcomes of patients who undergo LLR remain unanswered. One potential hypothesis is that the incidence rate of GDA is 47%, and that most of the cases improved spontaneously by the 4th postoperative day. Conversely, it is suggested that patients with GDA that lasted more than 5 days may develop severe pneumonia. In fact, mild-to-severe pneumonia was observed in all 4 patients with moderate or severe complications (Clavien–Dindo classification II to IV) in the present study. Furthermore, the literature reports that diabetes mellitus is a risk factor for infectious complications, including pneumonia, after hepatic resection [23,24]. Indeed, the present study showed that the proportion of patients with diabetes mellitus was higher in the GDA group than in the group without GDA. In conclusion, we found that a GDA duration of 5 days or more may be a useful predictor of postoperative complications, and that this predictor should be assessed to improve the short-term outcomes of patients undergoing LLR. Therefore, we assume that early termination of bed rest, including the start of respiratory rehabilitation, and early improvements in GDA are crucial for the prevention of complications, including pneumonia. The present study has limitations; it was a retrospective single-center study with a relatively small sample size. Further research, including respiratory dynamics during surgery, is also needed on the detailed mechanism of GDA generated by the intraoperative left half lateral position.

Abbreviations

LLR: laparoscopic liver resection

GDA: gravity-dependent atelectasis

OR: odds ratio

BMI: body mass index

ASA: American Society of Anesthesiologists

CIs: confidence intervals

Declarations

Ethics approval and consent to participate

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee (#2020-1115) and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all individual participants included in the study.

Consent to publish

Informed consent was obtained from all individual participants included in the study.

Availability of data and materials

The datasets used and analyzed during the current study are available from the corresponding author upon reasonable request.

Competing interests

The authors declare that they have no conflicts of interest.

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This study had no funding.

Authors' Contributions

Study conception: MR, OT and TA; Study design: MR, OT, and TA; Data acquisition: MR and OT; Quality control of data and algorithms: MR, OT and TA; Data analysis and interpretation: MR, OT and TA; Statistical analysis: MR and TA; Manuscript preparation: MR; Manuscript editing: OT and TA; Manuscript review: All authors; Final approval of the article: all authors. All authors read and approved the final manuscript.

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