Original

Factors influencing prolonged mechanical ventilation after liver transplantation: a retrospective cohort study

Hiroto Kurihara¹⁾, Motoi Kumagai¹⁾, Takashi Kobayashi¹⁾, Masahiro M Wakimoto¹⁾, Hirokatsu Katagiri²⁾, Hiroyuki Nitta²⁾ and Kenji S Suzuki¹⁾

> ¹⁾ Department of Anesthesiology, School of Medicine, Iwate Medical University, Yahaba, Japan

²⁾Department of Surgery, School of Medicine, Iwate Medical University, Yahaba, Japan

(Received on December 27, 2021 & Accepted on February 24, 2022)

Abstract -

To examine the factors contributing to the prolongation of the mechanical ventilation period after liver transplantation, we retrospectively inspected adult living donor liver transplant recipients.

A total of 46 adult liver failure patients who had undergone liver transplantation from a living donor were enrolled in this study. The subjects were divided into two groups based on the postoperative mechanical ventilation period: Group 1 comprised patients who had left within 24 hours of the postoperative ventilator use (n = 33), and Group 2 consisted those who had been mounted on a ventilator for over 24 hours after surgery (n = 13).

The duration of mechanical ventilation was 11.0 (9.2, 12.0) hours in Group 1 and 36.5 (33.0, 154.0)

hours in Group 2. Group 1 had younger patients and more men than Group 2 (p < 0.05). There were no significant differences in pre-anesthetic laboratory data except for the serum aspartate aminotransferase level between the two groups, but hemoglobin concentration and hematocrit at the end of surgery were significantly higher in Group 2 (p <0.05). The patient's age, sex, and hematocrit at the end of surgery affected the postoperative duration of mechanical ventilation in the regression analysis (p <0.05).

Older age, female sex and high value of hematocrit at the end of surgery were factors of longer postoperative mechanical ventilation period in liver transplant patients.

Key words : liver transplantation, mechanical ventilation, hematocrit, hemoglobin concentration

I. Introduction

Liver transplantation is one option with endstage liver diseases, but the results of postoperative outcomes are not always satisfactory ¹⁻³⁾.

Corresponding author: Kenji S Suzuki kenjis@iwate-med.ac.jp One of the causes of poor convalescence is postoperative respiratory failure. Transplant patients are usually taken off mechanical ventilation and extubated in the early morning of postoperative day 1. However, some patients often experienced difficulty separating from mechanical ventilation. Various reasons for



Fig. 1. Flowchart of eligible included in the study

prolonging mechanical ventilation have been previously reported ⁴⁻⁷⁾, including respiratory failure before the operation and renal disturbance. To examine the factors contributing to the prolongation of the mechanical ventilation period after liver transplantation, we retrospectively inspected adults who received liver transplants from living donors. In addition, underlying factors of the respiratory failure after the operation of liver transplantation should be detected, and it is necessary to make use in perioperative care.

II. Patients and methods

This study was approved by the Ethics Committee of Iwate Medical University School of Medicine (MH2018-043).

Clinical data of decompensated cirrhosis patients who had undergone liver transplantation from living donors between January

Abbreviations

PT-INR: prothrombin time-international normalized ratio aPTT: activated partial thromboplastin time ATIII: anti-thrombin III AST: aspartate aminotransferase ALT: alanine aminotransferase

2012 and March 2020 were obtained from electronic clinical records and anesthetic records. Patients under 16 years of age, those requiring reoperation, and those who died within 90 days of the procedure were excluded. A total of 46 patients were enrolled in this study.

All patients received fentanyl and/or remifentanil for pain prevention during general anesthesia. For sedation, anesthesia was induced by intravenous administration of propofol and maintained by inhalation of 0.5–1.0% of isoflurane or 3–6% of desflurane with 40–80% oxygen mixed with air. Rocuronium (0.2–0.4 mg/kg/h) was continuously administered as a muscle relaxant during anesthesia. We routinely prepared dopamine and noradrenaline as vasopressors and prostaglandin E1 for maintenance of transplanted liver perfusion. Anesthesia-related drugs and cardiovascular agents were administered at the discretion of

BUN: blood urea nitrogen MELD: model for end-stage liver disease MEAF: model for early allograft function ICU: intensive care unit PNI: prognostic nutritional index

	Group 1 (n=33)	Group 2 (n=13)	p value
Age (years)	46.3 ± 12.8	$55.0 \pm 10.6 *$	0.035
Sex (M/F)	19/14	3/10 *	0.035
Height (cm)	164.2 ± 10.1	158.7 ± 7.3	0.083
Weight (kg)	61.8 ± 12.4	63.7 ± 11.7	0.639
BMI	22.9 ± 4.0	25.1 ± 3.4	0.086
Indication diseases			0.240
Cholestatic diseases	6	3	
Hepatocellular diseases	23	6	
Vascular diseases	1	0	
Neoplastic diseases	1	0	
Acute liver failure	2	3	
Metabolic diseases	0	0	
Others	0	1	
Cholestatic diseases	6	3	

Table 1. Demographic profile

Values are mean ± S.D. or number. BMI, body mass index.

*: p < 0.05 vs. Group 1.

the anesthesiologist. Regarding the infusion management, we administered red blood cell concentrates so that hemoglobin concentration came into the range of 8-10g/dl. In addition, platelet concentrate was infused when platelet count was less than 40,000/mm³, and fresh frozen plasma was infused when PT-INR was more than 1.5.

The subjects were divided into two groups based on the length of postoperative mechanical ventilation period. Group 1 subjects were separated from ventilation within 24 hours of surgery (n = 33). Group 2 subjects had ventilation lasting more than 24 hours after surgery (n = 13) (Fig. 1). Extubation in the intensive care unit was based on the following criteria: patients' consciousness level was clear, PF ratio was 300 or more, and PaCO₂ was less than 50 mmHg under spontaneous breathing.

We collected data on patient characteristics, anesthesia throughout the period, bleeding and urine dose, infused fluid volume, and perioperative laboratory data, including pulmonary function, blood gas analysis, blood cell counts, and coagulation function. These data were compared between the two groups.

Statistical analyses were performed using SPSS version 22 (SPSS Inc., Chicago, IL, USA). The Shapiro-Wilk test was used to assess whether the data were normally distributed. Continuous data were expressed as median (interguartile range) or mean ± SD, and categorical variables were expressed as the number of patients. The Mann-Whitney U test or unpaired Student's t-test was used to compare continuous variables. Categorical data were assessed using a chi-square test. Logistic regression and Cox proportional hazard model were used to assess the multivariate analysis, in which the independent valuables were taken from the results of the univariate statistical comparison between two groups with significance level p < 0.05. Statistical significance was set at p < 0.05.

Table 2. Pre-anesthetic laboratory data

	Group 1 (n=33)	Group 2 (n=13)	p value
Pulmonary function			
%VC (%)	92.5 (81.5, 104.7)	89.9 (79.4, 93.6)	0.494
FEV_{10} (L)	2.76 (2.15, 3.42)	2.19 (2.04, 2.56)	0.219
$FEV_{1,0} \% (\%)$	81.9 (77.6, 84.5)	81.7 (79.8, 84.9)	0.882
Blood gas analysis			
P/F ratio	425.7 (361.1, 466.7)	372.9 (270.7, 441.7)	0.154
рH	7.48 (7.45, 7.49)	7.46 (7.43, 7.47)	0.233
Base excess (mEq/L)	1.35 (0.08, 2.23)	0.00 (-0.90, 2.90)	0.611
HCO_3^{-} (mEq/L)	25.0 (23.9, 26.8)	23.6 (21.9, 25.8)	0.220
Blood count			
Hemoglobin (g/dl)	10.0 (9.1, 11.0)	9.7 (8.2, 10.1)	0.435
Hematocrit (%)	30.7 (27.6, 33.0)	29.0 (24.0, 30.9)	0.400
Platelet (/mm ³)	84.5 (52.0, 109.8)	68.0 (56.0, 106.0)	0.861
Coagulation function			
PT-INR	1.39 (1.25, 1.58)	1.40 (1.19, 1.62)	0.723
aPTT (sec)	39.0 (33.6, 50.1)	37.7 (33.9, 43.8)	0.726
Fibrinogen (mg/dl)	268.0 (178.0, 294.0)	289.0 (190.0, 341.5)	0.520
Anti-thrombin III (%)	56.0 (42.0, 79.0)	57.0 (50.0, 84.0)	0.558
Liver function			
Total bilirubin (mg/dl)	2.00 (1.10, 6.60)	3.70 (1.30, 10.50)	0.335
AST (mg/dl)	41.0 (29.0, 60.0)	59.0 (46.0, 69.0) *	0.044
ALT (mg/dl)	34.0 (23.0, 48.0)	30.0 (20.0, 38.0)	0.652
Renal function			
Creatinine (mg/dl)	0.76 (0.58, 0.96)	0.81 (0.58, 0.98)	0.600
BUN (mg/dl)	14.3 (10.3, 16.4)	13.4 (9.3, 18.2)	0.970
Electrolytes			
Na (mEq/L)	135.0 (132.4, 139.0)	137.0 (133.0, 138.8)	0.599
K (mEq/L)	3.87 (3.60, 4.08)	3.80 (3.60, 4.06)	0.961
Cl (mEq/L)	105.0 (102.0, 107.0)	107.0 (103.0, 108.0)	0.433
Others			
Total protein (mg/dl)	6.50 (5.80, 7.00)	6.20 (5.60, 6.40)	0.201
Albumin (mg/dl)	2.80 (2.30, 3.30)	2.80 (2.70, 3.30)	0.516
Lymphocyte count (/mcl)	850.0 (480.0, 1210.0)	660.0 (620.0, 930.0)	0.874
PNI	33.6 (27.7, 39.5)	33.1 (30.2, 38.7)	0.807
Lactate (mmol/L)	1.60 (1.20, 2.10)	1.50 (1.40, 1.90)	0.820
MELD	12.08 (6.61, 16.17)	10.43 (8.51, 17.94)	0.457

Values are expressed as the median (interquartile range). *: p < 0.05 vs. Group 1.

VC, vital capacity; FEV, forced expiratory volume; PT-INR, prothrombin time-international normalized ratio; aPTT, activated partial thromboplastin time; AST, aspartate aminotransferase; ALT, alanine aminotransferase; BUN, blood urea nitrogen; PNI, prognostic nutritional index; MELD, model for end-stage liver disease.

III. Results

There were significant differences between Group 1 and Group 2 with respect to age and sex (p < 0.05), but not in height, weight, and BMI. Adaptation diseases of liver transplantation did not differ (Table 1).

The pre-anesthetic laboratory data are shown in Table 2. Preoperative nourishment status was

	Group 1 (n=33)	Group 2 (n=13)	p value
Operation time (min)	743.0 (672.0, 857.0)	775.0 (747.0, 844.0)	0.176
Anesthesia time (min)	848.0 (782.0, 980.0)	908.0 (870.0, 962.0)	0.329
Blood loss (g)	4197.0 (1983.0, 6809.0)	3663.0 (2253.0, 11234.0)	0.583
Urine output (ml)	1390.0 (875.0, 2220.0)	1840.0 (845.0, 2585.0)	0.687
Infusion volume (ml)	13210 (10330, 15130)	14260 (10180, 20680)	0.491
Total balance (ml/kg/hr)	8.76 (6.39, 11.50)	8.47 (6.39, 12.51)	0.950
Fentanyl dose (mcg/kg)	49.6 (26.6, 83.6)	40.1 (30.4, 71.4)	0.855
Infusion cotents (ml)			
Red cells concentrates	1680 (1120, 2240)	2240 (1400, 3360)	0.101
Fresh frozen plasma	2880 (1920, 4080)	3600 (2400, 5040)	0.241
Platelets concentrates	200 (0, 400)	400 (200, 600)	0.308
5% Albumin	4250 (3000, 6000)	4500 (3000, 7300)	0.582
Non-blood products	2750 (2400, 4200)	4500 (3000, 7300)	0.323
Bleeding dose – infusion volume of red cells concentrates (ml)	2625 (891, 4326)	1647 (1133, 5455)	0.798

Table 3. Intra-anesthetic data

Values are expressed as the median (interquartile range).

evaluated using the prognostic nutritional index (PNI), and the only significant difference involved the serum aspartate aminotransferase (AST) level.

Intra-anesthetic data involving fluid balance are presented in Table 3. The durations required for surgery and anesthesia were not statistically different, and there was no difference in the administered fentanyl dose. In addition, there were no differences in the fluid balance, or doses of blood preparations.

Laboratory data at the end of the surgery are shown in Table 4. The hemoglobin concentration and hematocrit were significantly lower in Group 1 (p < 0.05).

Thirteen of 46 patients (28.3%) required mechanical ventilation for over 24 hours. The duration of mechanical ventilation was 11.0 (9.2, 12.0) hours in Group 1 and 36.5 (33.0, 154.0) hours in Group 2. However, there were no statistical differences in the intensive care unit admission period and postoperative hospital stay between the two groups (Table 5).

Logistic regression analysis and Cox regression analysis were performed on the factors with p-values less than 0.05 in the comparison between the groups. The factors were the patients' age, sex, and serum concentration of AST as pre-anesthetic factors, and hemoglobin concentration and hematocrit as postoperative factors. The hemoglobin concentration at the end of surgery was excluded from the regression analysis because it was significantly correlated with the hematocrit value (p < 0.05). The patients age, sex, and hematocrit at the end of surgery affected the postoperative duration of mechanical ventilation (p < 0.05, Table 6, 7).

Figures 2 and 3 show the receiver operating characteristic (ROC) curve of the patients age and the hematocrit value at the end of surgery. The areas under the curve (AUC) were 0.65 for the patients age and 0.53 for the hematocrit value.

Hiroto KURIHARA, et al.

Table 4. Laboratory data at the end of surgery

	Group 1 (n=33)	Group 2 (n=13)	p value
Blood gas analysis			
P/F ratio	405.9 (361.2, 433.7)	349.8 (211,6, 416.7)	0.121
рН	7.42 (7.37, 7.43)	7.38 (7.35, 7.43)	0.335
Base excess (mEq/L)	-0.20 (-2.15, 0.68)	-0.70 (-4.90, 1.10)	0.634
HCO_3 (mEq/L)	24.1 (23.0, 25.2)	24.2 (21.6, 25.1)	0.900
Blood count			
Hemoglobin (g/dl)	8.8 (7.8, 9.7)	9.8 (8.9, 10.8) *	0.013
Hematocrit (%)	26.0 (23.0, 28.2)	29.0 (26.0, 32.0) *	0.010
Platelet (/mm³)	71.0 (60.0, 98.5)	71.0 (44.0, 82.0)	0.335
Coagulation function			
PT-INR	1.54 (1.42, 1.71)	1.45 (1.32, 1.52)	0.097
aPTT (sec)	43.7 (39.1, 50.9)	42.3 (39.1, 52.6)	0.920
Fibrinogen (mg/dl)	138.0 (114.0, 169.0)	162.5 (117.5, 216.0)	0.378
Anti-thrombin III (%)	66.0 (56.0, 88.0)	73.0 (58.0, 80.0)	0.999
Liver function			
Total bilirubin (mg/dl)	3.90 (3.20, 5.40)	4.50 (2.80, 7.90)	0.788
AST (mg/dl)	370.0 (240.0, 588.0)	389.0 (334.0, 589.0)	0.652
ALT (mg/dl)	248.0 (190.0, 511.0)	328.0 (191.5, 445.8)	0.950
Renal function			
Creatinine (mg/dl)	0.84 (0.57, 1.24)	0.80 (0.67, 1.38)	0.687
BUN (mg/dl)	14.3 (10.9, 18.9)	13.3 (9.4, 22.4)	0.802
Electrolytes			
Na (mEq/L)	142.0 (139.1, 143.9)	142.0 (139.0, 145.2)	0.841
K (mEq/L)	3.56 (3.29, 3.78)	3.61 (3.38, 3.90)	0.679
Cl (mEq/L)	107.0 (104.8, 110.0)	106.0 (103.0, 109.0)	0.707
Others	5.20 (4.90, 5.70)	5.10 (4.80, 6.30)	0.960
Total protein (mg/dl)			
Albumin (mg/dl)	3.85 (3.58, 4.30)	3.90 (3.70, 4.70)	0.539
Lactate (mmol/L)	4.45 (3.09, 6.65)	4.82 (3.41, 5.68)	0.767
MELD	15.49 (13.26, 18.92)	12.24 (11.03, 16.01)	0.550

Values are expressed as the median (interquartile range). *: p < 0.05 vs. Group 1.

PT-INR, prothrombin time-international normalized ratio; aPTT, activated partial thromboplastin time; AST, aspartate aminotransferase; ALT, alanine aminotransferase; BUN, blood urea nitrogen; MELD, model for end-stage liver disease.

IV. Discussion

Although liver transplantation for patients with end-stage liver disease has become a life-saving procedure in Japan, perioperative care for recipients has not yet been established, and patients' outcomes are not always satisfactory¹⁻³. One serious complication in perioperative care is respiratory failure, which may be due to difficulty in separating from mechanical ventilation. Furthermore, prolonging artificial ventilation and tracheal intubation can easily be accompanied by respiratory complications, such as pneumonia. It can also cause muscle weakness because the long-term artificial ventilation management disturbs progress of the rehabilitation ⁸⁻¹¹. In this study, we investigated the administrative factors of preoperative conditions and intraoperative anesthesia management as causes of prolonged

Table 5. Postoperative clinical course			
	Group 1 (n=33)	Group 2 (n=13)	p value
Time on ventilator (hours)	11.0 (9.2, 12.0)	36.5 (33.0, 154.0)	-
ICU stay (days)	10.0 (7.0, 15.0)	12.0 (9.0, 22.0)	0.182
Hospital stay (days)	60.0 (40.8, 98.0)	94.0 (57.0, 115.0)	0.234

able 5. Postoperative clinical course

Values are expressed as the median (interquartile range).

ICU, intensive care unit.

Table 6. Multivariate logistic regression analysis for postoperative longer mechanical ventilation

	OR	95% CI	p value
Age *	1.098	1.011-1.193	0.027
Sex *	9.061	1.361-60.337	0.011
Hematocrit value at the end of surgery *	1.278	1.039-1.572	0.020

*: p < 0.05.

Table 7. Cox regression analysis for postoperative longer mechanical ventilation

	Group 1 (n=33)	Group 2 (n=13)	p value
Age *	0.967	0.940-0.996	0.024
Sex *	0.419	0.199-0.879	0.021
Hematocrit value at the end of surgery *	0.909	0.836-0.989	0.026

*: p < 0.05.



Fig. 2. Receiver operating characteristic (ROC) curve for prolonged mechanical ventilation after liver transplantation on patients' age. Area under the curve (AUC) is 0.63.



Fig. 3. Receiver operating characteristic (ROC) curve for prolonged mechanical ventilation after liver transplantation on the hematocrit value at the end of surgery. Area under the curve (AUC) is 0.55.

mechanical ventilation.

Avolio et al. demonstrated that the predictors of postoperative respiratory failure were a higher value of Model for End-stage Liver Disease (MELD) score, restrictive lung pattern, intraoperative veno-venous bypass, high PaCO₂ before extubation, and Model for Early Allograft Function (MEAF) in non-acute liver transplantation⁴. Their diagnosis of postoperative respiratory failure included patients who needed artificial ventilation after surgery for more than 48 hours, with 36.0% of the cases meeting these criteria. In contrast, in the present study, 8.7% of the patients required mechanical ventilation management for more than 48 hours after surgery. One possible reason for the difference is that we excluded reoperation cases and cases of mortality within 90 days of surgery to evaluate only respiratory function in the early period after the first transplantation surgery. In addition, the criteria for weaning from mechanical ventilation in our facilities might differ from those of other facilities.

None of the patients in this study had preoperative pulmonary complications related to end-stage liver failure, including hepatic hydrothorax, hepatopulmonary syndrome, porto-pulmonary hypertension, and a -1antitripsin deficiency emphysema⁵. In addition, there were no significant differences between the groups in preoperative pulmonary oxygenation ability. Therefore, it is thought that the prolongation of the postoperative artificial ventilation period in our study was mainly influenced by factors involved in anesthesia management. Several other studies have shown that older patients, women, and patients with hepatic functional reserve, history of lung disease, renal impairment, the merger of diabetes, and the state of the donor's liver are preoperative factors associated with respiratory failure ^{4, 5, 12)}. It is difficult to compare these studies directly because the pathologic diagnostic criteria were different for each facility, and the perioperative care of liver transplantation was different.

Respiratory complications in the early period after liver transplantation include pulmonary edema, pleural effusion, atelectasis, pneumonia, and transfusion-related acute lung injury. Perioperative respiratory complications are one of the causes of poor outcomes in liver transplant patients ^{4, 5, 8)}. Our results showed that there were significant differences in preanesthetic factors such as patients' age, sex, and serum AST level, whereas hemoglobin concentration and hematocrit value at the end of surgery were intraoperative factors between the groups (p <0.05). These factors were regarded as influencing muscular strength in elderly people. Female patients experienced prolongation of artificial ventilation, and since the normal value of serum creatinine concentration was lower in female patients, it was considered that the MELD score was underestimated ^{11, 12}. In this study, when the creatinine level of a woman was multiplied by 1.2, the difference between the groups increased, but it was not significant; Group 1: 0.77 (0.65, 0.98), Group 2: 0.88 (0.70, 1.08). There was an apparent difference in the preoperative serum AST level between the groups, but it was not an influencing factor that was meaningful in the regression analysis. A possible reason why the preoperative AST was significantly higher in Group 2 could be that more AST was derived from other organs and organizations, including the kidney. This is because the ALT, which is specific to the liver, was slightly higher in Group

1. The regression analysis revealed that older age, female sex, and higher hematocrit values at the end of surgery were factors that extended the mechanical ventilation periods (p < 0.05). The high hematocrit value may be able to produce a disorder of blood flow in the transplanted liver because of the hyper viscosity of the blood ¹³. In addition, surplus blood transfusion may cause lung edema by increasing fluid preload to the heart and transfusion-related acute lung injury ⁴⁾. Sahinturk et al. reported that preoperative presence of hepatic encephalopathy, high AST level, large intraoperative infused dosage of red blood cell preparation, and longer duration of surgery were predictive factors of postoperative prolonged artificial ventilation period¹⁴⁾.

Many studies on the prognostic factors of liver disease have been published, but there have been no reliable studies so far ¹⁵⁻¹⁸. The MELD score is a representative index of liver damage with MELD-Na and MELDlactate ¹⁹⁻²². Recently, in addition to the MELD score, the MEAF score and liver graft assessment following the transplantation risk score have been reported to be more accurate predictors of transplanted liver function ^{23, 24}. Furthermore, lactate clearance has been demonstrated to be useful in predicting early graft dysfunction after surgery ²⁵⁻²⁸.

In the present study, we assessed the cause of early postoperative respiratory failure from the perspective of pre- and intra-anesthesia factors. Although the preanesthetic laboratory data, except for serum AST concentration, did not differ between groups, it was significantly different for the patients' age and sex (Tables 1 and 2, p < 0.05). Meanwhile, there were differences in hemoglobin concentration and hematocrit at the end of surgery between the groups (Table 4, p < 0.05). Moreover, the patients' age, sex, and hematocrit at the end of surgery had effects on the early postoperative respiratory condition (Table 6, 7, p < 0.05). This means that increased age, female sex, and surplus blood transfusion during surgery are risk factors for prolonged postoperative mechanical ventilation. Although there were no statistical differences in the infusion volumes of blood-derived products during anesthesia, differences in the quantity of blood loss and red blood cell preparation were slightly lower in Group 2 (Table 3). Anesthesiologists should be careful with fluid management, especially with blood transfusions during liver transplant surgery.

About ROC curve (Fig. 2, 3), it was a little higher for patients' age, but this cannot be said to be highly accurate based on ROC for both parameters because the $0.5 \sim 0.7$ of AUC is a low level of accuracy. When we assumed a cutoff of 55 years of age, 44% of sensitivity and 82% of specificity predicted that artificial ventilation periods would become more than 24 hours. While we assumed a cut-off level of 35% of the hematocrit value at the end of surgery, 75% of sensitivity and 76% of specificity predicted that artificial ventilation periods would be more than 24 hours.

There have been reports that the risk of complications in liver failure patients is greater in patients with a MELD score \geq 18, and their risk of post-liver transplantation is higher ¹⁵⁻¹⁷. On the other hand, patients with higher MELD scores are indicated for liver transplantation, and there are cases in which it is the only life-saving option.

The most important finding in this study

was that higher values of hematocrit and/or hemoglobin concentration at the end of liver transplantation affected the length of artificial ventilation required by the patients.

This retrospective study has some inherent limitations. First, the number of patients was small, and the groups were of different sizes. Second, the patients were divided into two groups based on the duration of the postoperative mechanical ventilation period. In the present study, we selected 24 hours after surgery as the criterion because ventilatory weaning is usually performed on the day after the operation. However, it is unclear whether our classification was adequate. Third, we did not analyze donor graft quality.

The number of liver transplantations in Japan, especially from brain-dead donors, remains small compared to that in Europe or the US because the concept of brain death has not permeated Japanese society. However, the total number of operations has steadily increased. Therefore, further analyses of Japanese liver transplantation are necessary. In conclusion, the results of our study have shown that liver transplant patients who are older, women or have higher hematocrit values at the end of surgery are more likely to need a longer postoperative mechanical ventilation period. Anesthesiologists should be careful with fluid management, especially blood transfusions during liver transplant surgery, to prevent prolonged mechanical ventilation.

Declarations

Authors' contributions: KSS designed the study. HK prepared most of the manuscript and analyzed and interpreted the data. All authors have taken charge of anesthetic management and contributed to writing the manuscript for submission.

Ethics approval and consent to participate: This was a retrospective cohort study, and the study was approved by the Ethics Committee of Iwate Medical University School of Medicine (approval number: MH2018-043).

Conflict of interest: The authors have no conflict of interest to declare.

References

- Jochmans I, van Rosmalen M, Pirenne J, et al.: Adult liver allocation in Eurotransplant. Transplantation 101, 1542-1550, 2017.
- 2) Togashi J, Sugawara Y, Akamatsu N, et al.: Quality of life after adult living donor liver transplantation: a longitudinal prospective followup study. Hepatol Res 43, 1052-1063, 2013.
- 3) Yamashiki N, Sugawara Y, Tamura N, et al.: Outcomes after living donor liver transplantation for acute liver failure in Japan: results of a nationwide survey. Liver Transpl 18, 1069-1077, 2012.
- 4) Avolio AW, Gaspari R, Teofili L, et al.: Postoperative respiratory failure in liver transplantation: Risk factors and effect on prognosis. PLOS ONE 14, e0211678, 2019.
- 5) Cardoso FS and Karvellas CJ: Respiratory

complications before and after liver transplant. J Intensive Care Med **34**, 355-363, 2019.

- Kleine M, Vondran FWR, Johanning K, et al.: Respiratory risk score for the prediction of 3-month mortality and prolonged ventilation after liver transplantation. Liver Transpl 19, 862-871, 2013.
- 7) FeltraccoP, Carollo C, Barbieri S, et al.: Early respiratory complications after liver transplantation. World J Gastroenterol 19, 9271-9281, 2013
- Kramer DJ, Siegal EM, Frogge SJ, et al.: Perioperative management of the liver transplant recipient. Crit Care Clin 35, 95-105, 2019.
- 9) Wieske L, Witteveen E, Verhamme C, et al.: Early prediction of intensive care unit-acquired weakness using easily available parameters: A

prospective observational study. PLOS ONE 9, e111259, 2014.

- Hill AD, Fowler RA, Burns KEA, et al.: Longterm outcomes and health care utilization after prolonged mechanical ventilation. Ann Am Thorac Soc 14, 355-362, 2017.
- 11) Yang T, Li Z, Jiang L, et al.: Risk factors for intensive care unit-acquired weakness: A systematic review and meta-analysis. Acta Neurol Scand 138, 104-114, 2018.
- 12) Wang A, An X and Xia VW: Female gender of the recipient is independently associated with prolonged ventilation time and hospital stay after liver transplantation. Transplant Proc 48, 120-122, 2016.
- 13) Debbaut C, Monbaliu D, Casteleyn C, et al.: From vascular corrosion cast to electrical analog model for the study of human liver hemodynamics and perfusion. IEEE Trans Bio Med Eng 58, 25-35, 2011.
- 14) Sahinturk H, Ozdemirkan A, Zeyneloglu P, et al.: Risk factor for postoperative prolonged mechanical ventilation after pediatric liver transplantation. Exp Clin Transplant 9, 943-947, 2021
- 15) Rutherford A, King LY, Hynan LS, et al.: Development of an accurate index for predicting outcomes of patients with acute liver failure. Gastroenterology 143, 1237-1243, 2012.
- 16) McPhail MJ, Farne H, Senvar N, et al.: Ability of King' s college criteria and model for endstage liver disease scores to predict mortality of patients with acute liver failure: a meta-analysis. Clin Gastroenterol Hepatol 14, 516-525, 2016.
- 17) Peng Y, Qi X and Guo X: Child-Pugh versus Score for the Assessment of Prognosis in Liver Cirrhosis: A systematic review and meta-analysis of observational studies. Med (Baltim) 95, e2877, 2016.
- 18) Reddy SS and Civan JM: From Child-Pugh to model for end-stage liver disease: Deciding who needs a liver transplant. Med Clin North Am 100, 449-464, 2016.
- 19) Cardoso NM, Silva T, Basile-Filho A, et al.: A new formula as a predictive score of post-liver

transplantation outcome: postoperative MELDlactate. Transplant Proc **46**, 1407-1412, 2014.

- 20) Barreto AG, Daher EF, Silva Junior GB, et al.: Risk factors for acute kidney injury and 30-day mortality after liver transplantation. Ann Hepatol 14, 688-694, 2015.
- 21) Sundaram V, Jalan R, Wu T, et al.: Factors associated with survival of patients with severe acute-on-chronic liver failure before and after liver transplantation. Gastroenterology 156, 1381-1391, 2019.
- 22) Kim S, Zerillo J, Tabrizian P, et al.: Postoperative meld-lactate and isolated lactate values as outcome predictors following orthotopic liver transplantation. Shock 48, 36-42, 2017.
- 23) Pareja E, Cortes M, Hervás D, et al.: A score model for the continuous grading of early allograft dysfunction severity. Liver Transpl 21, 38-46, 2015.
- 24) Agopian VG, Harlander-Locke MP, Markovic D, et al.: Evaluation of early allograft function using the liver graft assessment following transplantation risk score model. JAMA Surg 153, 436-444, 2018.
- 25) Kim DG, Lee JY, Jung YB, et al.: Clinical significance of lactate clearance for the development of early allograft dysfunction and short-term prognosis in deceased donor liver transplantation. Clin Transplant 31, https://doi. org/10.1111/ctr.13136, 2017.
- 26) Perilli V, Aceto P, Sacco T, et al.: Usefulness of postreperfusion lactate clearance for predicting early graft recovery in liver transplant patients: A single center study. Minerva Anestesiol 84, 1142-1149, 2018.
- 27) Golse N, Guglielmo N, El Metni A, et al.: Arterial lactate concentration at the end of liver transplantation is an early predictor of primary graft dysfunction. Ann Surg 270, 131-138, 2019.
- 28) Hatakeyama T, Hongo S, Kumagai M, et al.: Intraoperative increased plasma lactate concentration as a prognostic factor for liver transplant recipients: a retrospective cohort study. JIMA 73, 1-11, 2021.

岩手医誌 74 巻, 4 号 (令和 4 年 10 月) 153-164 頁.

生体肝移植レシピエントの 術後人工呼吸長期化に影響を与える因子 -後向きコホート研究-

栗原寬人¹⁾, 熊谷 基¹⁾, 小林隆史¹⁾, 脇本将寬¹⁾, 片桐弘勝²⁾, 新田浩幸²⁾, 鈴木健二¹⁾

¹⁾ 岩手医科大学医学部,麻酔学講座
²⁾ 岩手医科大学医学部,外科学講座

(Received on December 27, 2021 & Accepted on February 24, 2022)

要旨

肝移植レシピエント患者において,術後人工呼吸時 間に影響する因子を明らかにする目的で後ろ向きに検 討した.

当施設で施行された生体肝移植術レシピエント患者 46名を対象とし、術後24時間以内に人工呼吸を離脱 した患者:1群(n = 33)と24時間以上の人工呼吸管 理を要した患者:2群(n = 13)に振り分け、患者背 景および周術期データについて群間比較した。

2群と比較して1群患者は年齢が低く,男性が多かった(p<0.05).術前検査データでは,血中AST

濃度が2群で高かった (p < 0.05). 手術終了時の検査 データでは、ヘモグロビン濃度およびヘマトクリット 値が2群で高かった (p < 0.05). 群間比較にて有意差 を認めた因子による重回帰分析では、年齢・性別・手 術終了時のヘマトクリット値が術後人工呼吸時間に影 響を与える因子であった (p < 0.05).

高齢・女性・手術終了時のヘマトクリット値高値は 肝移植において術後人工呼吸時間を延長させる因子で あることが示唆された.