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# Retrospective Comparative Study on Postoperative Pulmonary Complications After Orthotopic Liver Transplantation Using the Melbourne Group Scale (MGS-2) Diagnostic Criteria

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**Background:** Postoperative pulmonary complications (PPCs) after orthotopic liver transplantation (OLT) are associated with poor postoperative survival. However, there are no standard criteria for diagnosis of PPCs. This retrospective study aimed to explore the reliability of the Melbourne Group Scale version 2 (MGS-2) for determining PPCs after OLT.

**Material/Methods:** A total of 121 patients were divided into 3 groups. In the PPC and non-PPC groups, PPCs were determined to be present or absent in accordance with both the MGS-2 and the conventional broad criteria for diagnosis of PPCs; in the potential-PPC group, PPCs were determined to be present only in accordance with the conventional broad criteria. The perioperative risk factors for PPCs and prognosis of patients in potential-PPC group were all compared with non-PPC groups and PPC groups.

**Results:** The preoperative characteristics of patients in the potential-PPC group were similar to those in non-PPC group. The length of intensive care unit stay ( $2.26 \pm 0.22$  vs.  $4.75 \pm 0.47$  days;  $P=0.017$ ), duration of hospitalization ( $33.33 \pm 1.70$  vs.  $48.78 \pm 2.53$  days;  $P<0.001$ ), and treatment cost ( $28.01 \pm 1.78$  vs.  $38.35 \pm 1.85 \times 10\ 000$  yuan;  $P=0.018$ ) were significantly less in the potential-PPC group than in the PPC group. Furthermore, in accordance with the MGS-2 criteria for diagnosis of PPCs, patients with PPCs showed poorer overall survival rates than those without ( $P=0.038$ ).

**Conclusions:** The MGS-2 appears to be a more suitable and reliable tool for diagnosis of PPCs and to identify the post-OLT patients with poorer perioperative characteristics and prognosis.

**MeSH Keywords:** Liver Transplantation • Lung • Postoperative Complications • Survival Rate

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## Background

Postoperative pulmonary complications (PPCs) after orthotopic liver transplantation (OLT) – especially those occurring within the first month after surgery – are significantly associated with poor postoperative survival [1]. Using conventional broad criteria for diagnosis of PPCs, any postoperative pulmonary abnormality that adversely affects the clinical course of a patient could be defined as a PPC, including respiratory failure, pneumonia, atelectasis, pneumothorax, pleural effusion, acute lung injury (ALI), acute respiratory distress syndrome (ARDS), and various other forms of upper airway obstruction [2–4]. Previous studies have reported varying incidences of PPCs after liver transplantation, ranging from 42.1% to 86.7%, in accordance with broad diagnostic criteria; the corresponding fatality rates have been reported to be 25% to 52.9% [5,6]. In addition, it was also reported that some PPCs, such as pleural effusion, were non-fatal and had better clinical prognosis than the fatal ones, like ARDS [7]. Multiple studies have focus on the prevention and treatment of OLT-induced PPCs, but it is difficult to comparatively evaluate the effect of PPCs on post OLT outcomes in different studies because of differences in diagnostic criteria. Therefore, objective definition, as well as a tool for accurate diagnosis of PPCs, are important for predicting prognosis and guiding interventions.

The Melbourne Group Scale version 2 (MGS-2) was designed to help senior physiotherapists perform routine respiratory assessments [8]. However, no study to date has employed the MGS-2 for identifying the development of PPCs after OLT. Thus, this retrospective study was conducted to explore the clinical reliability of the MGS-2 in comparison with that of the conventional broad criteria for determining PPCs after OLT.

## Material and Methods

### Study design

This retrospective study was approved by the Ethics Committee of the Third Affiliated Hospital of Sun Yat-Sen University and was performed in compliance with the Declaration of Helsinki. The requirement for informed consent was waived because the study was retrospective in nature and employed data in which patient identification information had been removed. Donor organs were procured through the Red Cross society in Guangdong province. Both donors and recipients provided consents.

This retrospective cohort study was designed to explore the reliability of the MGS-2 for determining PPCs after OLT, comparing with the “conventional broad criteria”. Two criteria are used for simultaneous diagnosis. Patients were divided into the

following 3 groups: PPC, non-PPC, and potential-PPC groups. In the PPC group, patients were diagnosed PPCs in accordance with both the MGS-2 and the conventional broad criteria. In the non-PPC group, no PPCs were diagnosed according to both diagnostic criteria. In the potential-PPC group, PPCs were diagnosed only according to the conventional broad criteria. All pulmonary complications of participants were independently diagnosed by 2 doctors (Xiaoyun Li and Xiaoxia Wei). If the diagnoses of these 2 doctors were inconsistent in a particular case, a third doctor (Ziqing Hei) validated the diagnosis.

### Diagnostic criteria for early PPCs

The MGS-2 and the conventional broad PPC criteria were employed for diagnosis of PPCs occurring within a month after OLT. Details regarding the MGS-2 criteria are shown in Table 1. The MGS-2 was used to screen for the presence of PPCs until 1 or more PPCs were diagnosed; a PPC was diagnosed if 4 or more of the 8 factors were present. It was assumed that patients who were discharged from the hospital without PPC within the first month after surgery did not develop PPCs subsequently.

The “conventional broad criteria” for PPCs is a thorough list of pulmonary complications consisting of major to minor infectious and non-infectious pulmonary events occurring after surgery, including ALI, ARDS, atelectasis, pneumothorax, pleural effusion, and respiratory infections such as pneumonia [2–4]. Details regarding these conventional broad criteria are shown in Table 2.

### Participants

Medical records of patients who underwent OLT between May 2012 and September 2015 at the Third Affiliated Hospital of Sun Yat-Sen University were retrospectively reviewed. All patients between the ages of 18 and 65 years who underwent OLT with organs procured from deceased donors were considered for inclusion. The exclusion criteria were: 1) re-transplantation; 2) living-donor liver transplantation; 3) nonfunctional donor liver; 4) combined liver-kidney transplantation; 5) death within 24 h after surgery; 6) pediatric liver transplantation, and 7) incomplete clinical information for screening for PPCs. The exclusion criteria were all in accordance with earlier reports [2–4]. Clinical and epidemiological data of the included patients were collected using an electronic patient data recording system. All patients were adopted uniform immunosuppression protocol of our institution after operation, which concluded immunosuppression induction of basiliximab combined calcineurin inhibitor (CNI) and glucocorticoid.

**Table 1.** Melbourne Group Scale Version 2.

Criteria
<ul style="list-style-type: none"><li>• Temperature &gt;38°C</li><li>• White cell count &gt;11.2 or use of respiratory antibiotics</li><li>• Physician diagnosis of pneumonia or chest infection</li><li>• Chest X-ray findings of atelectasis/consolidation</li><li>• Production of purulent (yellow/green) sputum different from preoperative sputum</li><li>• Positive results upon sputum microbiological analysis</li><li>• SpO<sub>2</sub> &lt;90% in ambient air</li><li>• Re-admission to or prolonged stay (&gt;36 h) in the intensive care unit/high dependency unit for respiratory problems</li></ul>

SpO<sub>2</sub> – blood oxygen saturation level.

**Table 2.** Definitions of postoperative pulmonary complications.

The broad criteria of PPC
<b>Acute lung injury (ALI)</b> Acute onset of hypoxemia (partial pressure of oxygen, arterial [PaO <sub>2</sub> ]/fraction of inspired oxygen [FIO <sub>2</sub> ] ≤300 mmHg) with new bilateral infiltrates in the setting of either a normal pulmonary arterial wedge pressure (PAWP ≤18 mmHg) or the absence of suspected of left atrial hypertension when PAWP was not available
<b>Acute respiratory distress syndrome (ARDS)</b> ARDS is a special kind of ALI. In the setting of more severe hypoxemia (PaO <sub>2</sub> /FIO <sub>2</sub> ≤200 mm Hg), the term Acute respiratory distress syndrome (ARDS) was applied
<b>Pleural effusion</b> Chest radiograph demonstrating blunting of the costophrenic angle, evidence of displacement of adjacent anatomical structures, or (in supine position) a hazy opacity in one hemithorax with preserved vascular shadows
<b>Atelectasis</b> Collapse of the alveoli, lung opacification with shift of the mediastinum, hilum, or hemidiaphragm toward the affected area, and compensatory overinflation in the adjacent nonatelectatic lung
<b>Pneumothorax</b> A collection of air in the pleural space (the area with no vascular bed surrounding the visceral pleura)
<b>Respiratory infection</b> Treatment with antibiotics for a respiratory infection, plus at least one of the following criteria: new or changed sputum, new or changed lung opacities, fever, and leukocyte count >12,000/mm <sup>3</sup>

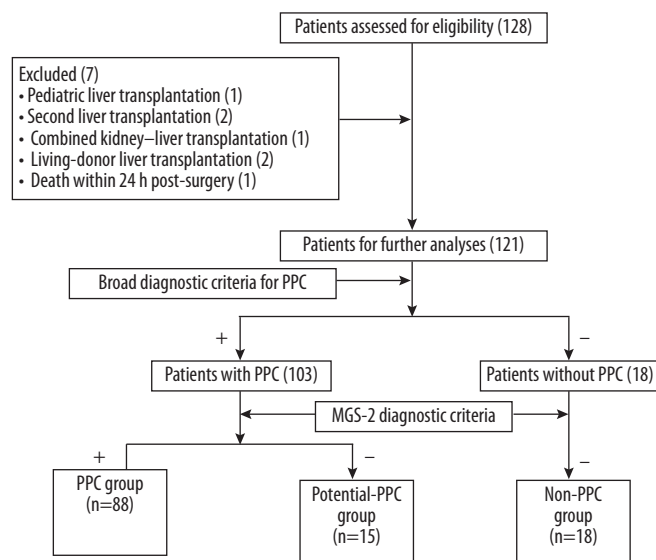
## Data collection

Data regarding patient demographics, liver biochemical findings, model for end-stage liver disease (MELD) score, and Child-Turcotte-Pugh (CTP) class before surgery were extracted. Intra- and postoperative clinical variables – including cold ischemia and warm ischemia time and volumes of infusion (red blood cells, plasma, cryoprecipitate, and crystalloid solution) and blood loss – were also recorded, as were the durations of ventilation after surgery, intensive care unit (ICU) stay, and hospitalization.

Survival time was defined as the interval between surgery and PPC-associated death or the end of October of 2016. Patients who died from other diseases were considered as lost to follow-up, and cases of survival at the end of October of 2016 were defined as censored data.

## Statistical analysis

Quantitative variables are presented as mean ± standard error (SE). Qualitative and ordinal data were presented as absolute frequencies. The one-sample Kolmogorov-Smirnov Test was used for testing the normality of quantitative data, and the independent-samples *t*-test and Wilcoxon rank-sum test were used for assessment of intergroup differences. The Pearson chi-square and Fisher's exact probability tests were used for comparison of qualitative data. Survival curves were analyzed using the Kaplan-Meier method, and the log-rank test was used for assessment of differences between subgroups. Univariable and multivariable logistic regression models were used for identifying potential risk factors for PPCs. Differences were considered significant at *P* values <0.05. Statistical analysis was performed using the Statistical Package for Social Sciences 19.0 software (SPSS Inc., Chicago, IL, USA).



**Figure 1.** Flow chart of the inclusion and exclusion processes. PPC – postoperative pulmonary complication.

## Results

A total of 132 patients who underwent OLT at our hospital were reviewed for inclusion. After excluding 11 patients who met at least 1 of the exclusion criteria, 121 patients were included for further analyses. There were 103 (103/121, 85.1%) patients deemed to have PPCs according to the conventional broad criteria, among which 88 (88/121, 72.7%) patients were also diagnosed to have PPCs when adjudged on the basis of the MGS-2 criteria (PPC group), so the remaining 15 patients were assigned to the potential-PPC group. Meanwhile, no PPCs were diagnosed according to both diagnostic criteria in the other 18 (18/121, 14.9%) patients (non-PPC group). The procedure for patient allocation and the details of the 3 groups are shown in Figure 1.

### Comparison of preoperative characteristics of the included patients

In order to prove the accuracy of the MGS-2 criteria, we tried to compare the pre-, intra-, and post-operative characteristics of patients in the potential-PPC group with those in the PPC and non-PPC groups; we found that the characteristics of patients in the potential-PPC group were more comparable to those in the non-PPC group (Table 3).

There were no significant differences among the 3 groups in terms of age distribution, sex, long-term smoking habit, or diabetes. The proportion of patients with a preoperative diagnosis of pulmonary diseases in the potential-PPC group (13.3%) was significantly lower than that in the PPC group (45.5%;  $P=0.019$ ) and comparable to that in the non-PPC group (16.7%;  $P=1.000$ ;

Table 3). Pneumonia and pneumonia accompanied by pleural effusion were the most commonly diagnosed preoperative pulmonary diseases, representing 80% of the preoperative lung disease burden among liver transplant recipients (Table 3).

There were no significant differences in indications for transplantation among the 3 groups. The overall proportion of patients with severe hepatitis and decompensated liver cirrhosis was 63.6%. The proportion of patients with preoperative MELD scores  $\geq 19$  points or CTP class C in the potential-PPC group was significantly lower than that in the PPC group and similar to that in the non-PPC group (Table 3). Serum albumin levels were higher in the potential-PPC group than in the PPC group ( $39.59 \pm 1.02$  vs.  $36.46 \pm 0.43$  g/L;  $P=0.006$ ; Table 3). There were no significant differences among the 3 groups in terms of white blood cell count or hemoglobin levels (Table 3).

### Comparison of intraoperative characteristics of the included patients

There were no significant differences among the 3 groups in terms of surgery-related variables, including operation method and times of anesthesia, cold ischemia, and warm ischemia (Table 3).

The proportions of patients with blood loss  $> 2$  L in the 3 groups were identical. However, the proportions of patients in the potential-PPC group with plasma transfusion volumes  $> 3000$  mL, total blood product transfusion volumes  $> 5000$  mL, and total infusion volume  $> 10$  L during surgery were comparable to those in the non-PPC group rather than to those in the PPC group (Table 3).

**Table 3.** Types and frequencies of PPCs in accordance with the broad criteria of diagnosis.

PPC	PPC group	Potential-PPC group	P value
ALI	18 (20.5)	0 (0)	0.119
ARDS	12 (13.6)	0 (0)	0.277
Atelectasis	16 (18.2)	3 (20)	0.848
Pneumothorax	5 (5.7)	0 (0)	1.000
Right	5 (5.7)	0 (0)	1.000
Left	0 (0)	0 (0)	1.000
Pleural effusion	84 (95.5)	12 (80)	0.100
Left	2 (2.3)	1 (6.7)	0.379
Right	24 (27.3)	5 (33.3)	0.864
Bilateral	58 (65.9)	6 (40)	0.0558
Respiratory infection	88 (100)	1 (6.7)	0.000
Fungal infection	21 (23.9)	0 (0)	0.076
Bacterial infection	48 (54.5)	1 (6.7)	0.005
Merging infection	12 (13.7)	0 (0)	0.335
Unclear etiology	7 (8.0)	0 (0)	0.564

Data are presented as number (percentage). PPC – postoperative pulmonary complication; ALI – acute lung injury; ARDS – acute respiratory distress syndrome.

### Comparison of postoperative characteristics of the included patients

The ventilation time in the potential-PPC group ( $15.83 \pm 2.73$  h) was significantly shorter relative to that in the PPC group ( $42.08 \pm 10.07$  h;  $P=0.013$ ) and comparable to that in the non-PPC group ( $13.25 \pm 2.77$  h; Table 3). However, there were no significant differences among the 3 groups in terms of postoperative fluid balance during the first 3 postoperative days (Table 3).

### Incidences of each complication in the potential-PPC group and the PPC group

To further explore the differences between the potential-PPC and PPC groups, the incidences of each complication in the potential-PPC group were compared with those in the PPC group. Patients in the PPC group were more likely to experience respiratory infections (100% vs. 6.7%;  $P<0.01$ ) and more than 2 types of PPCs (95.5% vs. 6.7%;  $P<0.01$ ) than those in the potential-PPC group (Table 4).

### Univariate and multivariate analysis of risk factors associated with PPC

As shown in Tables 3 and 4, the characteristics of patients in the potential-PPC group were more comparable to those in the non-PPC group, indicating that it might be meaningful to

identify the non-PPC patients using the MGS-2 criteria from those with poorer characteristics. To further explore the efficiency of MGS-2, univariate and multivariate logistic regression analyses were performed for comparison of characteristics between patients with (PPC group) and without (non-PPC and potential-PPC groups) PPCs in accordance with the MGS-2. The results of univariate regression analysis showed that some risk factors, including pre-existing lung disease, severity of liver dysfunction, and perioperative transfusion of red blood cells, were associated with PPCs diagnosed in accordance with the MGS-2 (Table 5). Upon multivariate regression analysis, preoperative MELD score  $\geq 19$  (OR=4.213; 95% confidence interval [CI]: 1.122–15.819) was found to be an independent risk factor for PPCs, and high preoperative albumin level (OR=0.876; 95% CI, 0.786–0.975) was found to be a protective factor against PPCs diagnosed on the basis of the MGS-2 (Table 5). However, multivariate logistic regression analysis did not reveal any independent factors associated with PPCs diagnosed in accordance with the conventional broad criteria.

### Prognosis between the 3 groups

The overall clinical outcomes of patients in the potential-PPC group were much better than those of patients in the PPC group (Table 6, Figure 2). The length of ICU stay ( $2.26 \pm 0.22$  vs.  $4.75 \pm 0.47$  days;  $P=0.017$ ), duration of hospitalization ( $33.33 \pm 1.70$  vs.  $48.78 \pm 2.53$  days;  $P<0.001$ ), and treatment cost

Table 4. Comparison of perioperative characteristics among the PPC groups.

	Potential-PPC group (n=15)	PPC group		Non-PPC group	
		(n=88)	P value	(n=18)	P value
<b>Preoperative variables</b>					
Age	49.53±1.70	47.52±1.14	0.484	48.67±1.97	0.750
Sex (male/female)	15/0	76/12	0.277	17/1	1.000
Long-term smoking habit	2 (13.3)	12 (13.6)	1.000	1 (5.6)	0.868
Preoperative lung disease Pneumonia	2 (13.3)	40 (45.5)	0.019	3 (16.7)	1.000
Pneumonia along with pleural effusion	0 (0)	15 (17.1)	0.182	1 (5.6)	1.000
Others	1 (6.7)	18 (20.5)	0.362	1 (5.6)	1.000
	1 (6.7)	7 (8.0)	0.727	1 (5.6)	1.000
Diabetes	1 (6.67)	11 (12.5)	0.829	2 (11.1)	1.000
<b>Indication of transplantation</b>					
Severe hepatitis	3 (20)	26 (29.5)	0.653	3 (16.7)	1.000
Decompensated liver cirrhosis	4 (26.7)	36 (40.9)	0.296	5 (27.8)	1.000
CTP class C	4 (26.7)	49 (55.7)	0.038	5 (27.8)	1.000
MELD score ≥19	0 (0)	28 (31.8)	0.025	1 (5.6)	1.000
WBC count > 11.2×10 <sup>9</sup> /L	0 (0)	11 (12.5)	0.319	0 (0)	/
Hemoglobin level <100 g/L	4 (26.7)	45 (51.1)	0.079	6 (33.3)	0.972
Albumin concentration	39.59±1.02	36.46±0.43	0.006	39.48±1.18	0.949
<b>Intraoperative variables</b>					
Operation method (piggyback)	14 (93.3)	84 (95.5)	1.000	15 (83.3)	0.733
Cold ischemia time, h	6.13±0.38	5.82±0.22	0.275	6.28±0.39	0.812
Anesthesia time, h	8.40±0.39	8.86±0.27	0.070	8.61±0.25	0.549
Operation time, h	6.79±0.42	7.39±0.20	0.117	7.00±0.37	0.568
Anhepatic time, min	42.87±3.77	46.47±1.91	0.232	44.89±3.33	0.637
RBC >18 units	4 (26.7)	47 (53.4)	0.056	4 (22.2)	1.000
Plasma volume >3000 mL	5 (33.3)	56 (63.6)	0.027	7 (38.9)	0.741
Cryoprecipitate >35 units	7 (46.7)	46 (52.3)	0.688	8 (44.4)	0.898
Transfusion blood product >5000 mL	7 (46.7)	70 (79.5)	0.017	11 (61.1)	0.407
Total volume of infusion >10 L	5 (33.3)	52 (59.1)	0.064	7 (38.9)	0.741
Blood loss >2 L	7 (46.7)	49 (55.7)	0.517	9 (50%)	0.849
<b>Postoperative variables</b>					
Ventilation time, h	15.83±2.73	42.08±10.07	0.013	13.25±2.77	0.645
ARI	0 (0)	23 (26.1)	0.056	0 (0)	/
<b>Postoperative fluid balance*</b>					
A	12 (80.0)	66 (75.0)	0.927	13 (72.2)	0.911
B	6 (40)	48 (54.5)	0.297	6 (33.3)	0.692
C	11 (73.3)	59 (67.0)	0.855	13 (72.2)	1.000
D	4 (26.7)	35 (39.8)	0.333	5 (27.8)	1.000

Data are presented as number (percentage) or mean ± standard deviation. PPC – postoperative pulmonary complication; CTP – Child-Turcotte-Pugh; MELD – model for end-stage liver disease; WBC – white blood cell; RBC – red blood cell; ARI – acute renal injury (renal injury was defined by serum creatinine concentrations >1.5 mg/dL or creatinine clearance levels <70 mL/min). \* Postoperative fluid balance – A: liquid balance on at least 1 of the first three postoperative days <–300 mL; B: liquid balance on at least 2 of the first three postoperative days <–300 mL; C: liquid balance on at least 1 of the first three postoperative days <–500 mL; D: liquid balance on at least 2 of the first three postoperative days <–500 mL.

**Table 5.** Significant risk factors associated with postoperative pulmonary complications according to the Melbourne Group Scale-2.

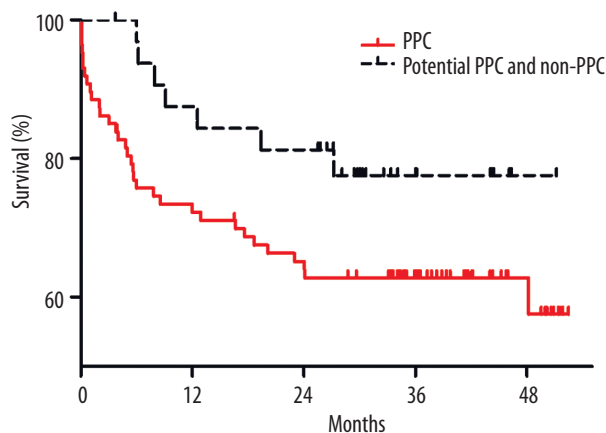
	Univariable analysis			Multivariable analysis		
	P value	OR	95% CI	P value	OR	95% CI
Bilirubin (umol/L)	0.002	1.005	1.002–1.008			
CTP Class C	0.007	3.350	1.398–8.029			
MELD score ≥19	0.001	8.333	2.367–29.344	0.033	4.213	1.122–15.819
Albumin concentration (g/L)	0.001	0.842	0.760–0.934	0.015	0.876	0.786–0.975
Hemoglobin level (g/L)	0.002	0.974	0.959–0.990			
International normalized ratio	0.003	4.017	1.601–10.076			
Infusion volume of RBC >18 units	0.005	3.582	1.457–8.807			

CI – confidence interval; OR – odds ratio; CTP – Child-Turcotte-Pugh; MELD – model for end-stage liver disease; RBC – red blood cells.

**Table 6.** Influence of early PPCs on clinical outcomes.

	Potential-PPC group (n=15)		PPC group n=88		P value	Non-PPC group n=18		
							P value	
Bronchoscopy sputum suction	0	(0)	13	(14.8)	0.241	0	(0)	/
Thoracentesis	3	(20)	24	(27.3)	0.784	0	(0)	0.167
Reintubation or tracheotomy	0	(0)	21	(23.9)	0.076	0	(0)	1.000
ICU stay, days	2.26±0.22		4.75±0.47		0.017	2.39±0.21		0.530
Hospital stay, days	33.33±1.70		48.78±2.53		<0.001	31.56±1.53		0.394
Cost, 10000 yuan	28.01±1.78		38.35±1.85		0.018	27.13±1.72		0.458
30-day survival	15	(100)	77	(87.5)	0.319	18	(100)	1.000
3-month survival	15	(100)	74	(84.1)	0.210	18	(100)	1.000
6-month survival	15	(100)	69	(78.4)	0.103	18	(100)	1.000
12-month survival	14	(93.3)	66	(75)	0.215	17	(94.4)	1.000

Data are presented as number (percentage) or mean ± standard deviation. PPC – postoperative pulmonary complication; ICU – intensive care unit.



**Figure 2.** Overall survival of the patients included in this study. PPC – postoperative pulmonary complication.

(28.01±1.78 vs. 38.35±1.85×10 000 yuan;  $P=0.018$ ) were significantly lower in the potential-PPC group than in the PPC group. There was no significant difference between the potential-PPC and non-PPC groups in terms of length of ICU stay, duration of hospitalization, or treatment cost (Table 6).

There were no significant differences in survival rate among the 3 groups. However, upon diagnosis on the basis of the MGS-2, patients who developed PPCs (PPC group) were found to exhibit lower 3-month, (84.1% vs. 100%;  $P=0.034$ ), 6-month (78.4% vs. 100%;  $P=0.004$ ), and 12-month (75% vs. 94.4%;  $P=0.016$ ) survival rates and overall survival rates ( $P=0.038$ ; Table 7, Figure 2) than patients without PPCs (potential-PPC and non-PPC groups). Upon diagnosis on the basis of the conventional broad criteria, there was no significant difference in overall survival rate between patients with (PPC and potential-PPC groups) and without (non-PPC group) PPCs ( $P=0.16$ ).

**Table 7.** Comparison of survival rate among early PPC groups classified in accordance with the MGS-2.

Survival duration	PPC group (n=88)	Non-PPC and potential-PPC groups (n=33)	P value
30 days	77 (87.5)	33 (100)	0.076
3 months	74 (84.1)	33 (100)	0.034
6 months	69 (78.4)	33 (100)	0.004
12 months	66 (75)	17 (94.4)	0.016

Data are presented as number (percentage). PPC – postoperative pulmonary complication; MSG-2 – Melbourne Group Scale version 2.

## Discussion

The present retrospective study, which involved patient data from a large medical center, comparatively evaluated the applicability of the MGS-2 and the conventional broad criteria for diagnosis of PPCs after OLT. We compared the pre-, intra-, and post-operative characteristics and prognosis of patients in the potential-PPC group with those in the PPC and non-PPC groups and found that the characteristics and prognosis of patients in the potential-PPC group were more comparable to those in the non-PPC groups. Univariate and multivariate regression analysis revealed that preoperative MELD score  $\geq 19$  was an independent risk factor for PPCs, and high preoperative albumin level was a protective factor against PPCs diagnosed on the basis of the MGS-2. The results suggested that the MGS-2 was more suitable and reliable than the conventional broad criteria for diagnosis of PPC in patients who had undergone OLT. To the best of our knowledge, the present retrospective single-center study is the first to evaluate the applicability of the MGS-2 as a diagnostic tool for early PPCs after OLT.

Although PPCs contribute to patient mortality and morbidity after OLT, a standard definition for PPCs has yet to be established. Therefore, any factor associated with dysfunction of normal lung endothelial-epithelial barriers or any other pulmonary abnormality is currently considered as a PPC in accordance with the broad diagnostic criteria [4]. In line with previous results [9–11], we also found that non-infectious pulmonary abnormalities, including pleural effusion and atelectasis, were the most frequent respiratory disorders after OLT. These non-infectious PPCs might be related to surgical maneuvers and have been reported to be usually self-limiting and respiratory physiotherapy might be unnecessary [6,11]. Moreover, our study indicated that 93.3% of complications in the potential PPC group involved self-limiting pulmonary abnormalities, including mostly pleural effusion and atelectasis. In this regard, most patients had good prognosis even though they were diagnosed as having PPCs in accordance with the conventional broad criteria. Thus, we suggest that patients with only these self-limiting pulmonary abnormalities might be excluded from a group of patients with PPCs following OLT by using

MSG-2 criteria. This might be a revolutionary thought in clinical practice since the MSG-2 criteria could provide better treatment guidance and evaluation of prognosis in patients with PPCs after OLT.

The MGS-2 was designed to help senior physiotherapists perform routine respiratory assessments [8]. Using this tool, PPCs are identified by 8 dichotomous factors on the basis of MGS-2 scores; PPCs are diagnosed if 4 or more of the 8 dichotomous factors are present. Because of its high validated interrater reliability, the MGS-2 has been used for determining the risk of PPCs in abdominal surgery [12]. The MGS-2 is likely to be more reliable than the conventional broad criteria for diagnosis of PPCs, because it uses 8 dichotomous factors based on the conventional broad criteria to determine the presence of PPCs. With the broad diagnostic criteria, pneumonia or chest infection is diagnosed by the physician solely on the basis of laboratory findings and symptoms manifested by the patient. In contrast, the MGS-2 comprehensively considers not only the preoperative and current pulmonary symptoms but also variables concerning subsequent treatment for respiratory problems, such as long ICU stay. Therefore, in comparison with the conventional broad criteria, the MGS-2 provides diagnoses that are more closely related to the prognoses of patients [8,13]. Moreover, in order to avoid bias, the MGS-2 requires the presence of at least 4 objective factors for determining PPCs. Because of this requirement for considering not only the clinical condition of the patients but also their laboratory findings, some self-limiting pulmonary abnormalities which might be easily cured and might not affect the prognosis could be excluded from PPCs diagnosed using the MGS-2 [14]. In previous studies that employed 8 variables for defining PPCs, the MGS-2 exhibited high interrater reliability in a thoracic surgery population and was used to identify the development of PPCs after abdominal surgery [14,15]. In line with these previous findings, the present results showed that the MGS-2 identified all cases of respiratory infection and 95.5% of cases with more than 2 types of PPCs in the PPC group. Patients with PPCs showed lower overall survival rates than those without PPCs according to the MGS-2 but not according to the conventional broad criteria.



Previous studies have reported some perioperative factors that predispose individuals to PPCs after OLT. Restrictive lung diseases and, especially, the degree of end-stage liver disease have been reported to be associated with PPCs [16,17]. Furthermore, MELD scores >25 have been shown to be associated with poor survival of patients or graft tissue, with maximum impact during the first year of transplantation [18]. Hypoalbuminemia is common among liver transplant recipients and has been shown to be associated with PPCs and mortality immediately after surgery [19]. Furthermore, recent studies have shown that hypoalbuminemia is associated with systemic inflammation, sepsis, and infection after surgery [20,21]. Patients with hypoalbuminemia are probably more susceptible to fluid overload and disruption of homeostasis and have been shown to be more likely to develop pneumonia or other infections relative to patients without this condition, probably because of their undernourished status and low immunity [22]. In the present study, with regard to these preoperative risk factors, patients in the potential-PPC group exhibited greater similarity to those in the non-PPC group than to patients in the PPC group. Furthermore, OLT is a lengthy procedure involving intraoperative factors – including massive intraoperative blood and fluid transfusion volumes – that are significant predictors of PPCs [11]. Excessive transfusion during OLT could lead to pulmonary edema, which could impair gas diffusion [23,24]. The results of the present study also showed that, relative to the potential-PPC and non-PPC groups, a greater proportion of patients in the PPC group received over 5 L of blood products and over 10 L of fluid transfusion. In particular, patients with high MELD scores and hypoalbuminemia might lack the capacity to handle such large volumes of fluid transfusion because they inevitably exhibit poor pulmonary gas exchange [25,26].

Accurate diagnosis of pulmonary complications will help guide the treatment process after liver transplantation. Ventilation time is not only a postoperative risk factor for PPCs but also a means for treatment of pulmonary complications. Early weaning from mechanical ventilation is known to favor good clinical outcomes [27]. The present findings demonstrated that patients diagnosed with PPCs in accordance with the MGS-2 not only experienced longer ventilation times and ICU and hospital stays and incurred greater treatment costs but also had shorter survival times than patients without PPCs. If patients

were to be diagnosed with PPCs as early as possible on the basis of the MGS-2, it might be possible to focus on necessary treatment for such patients instead of indiscriminate treatment such as using long-term ventilation and central catheterization, which carry a greater risk of infection. The results of our study suggest that application of the MGS-2 for evaluation of PPCs might help clinicians consciously avoid unnecessary and excessive medical treatment in order to improve the clinical outcomes of patients.

Several limitations of our study should be acknowledged. First, this was a retrospective study involving a small population, which limits the statistical power of the present results. Second, retrospective diagnosis of PPCs in accordance with the MGS-2 might lead to bias in the final analyses. We sought to address this possibility by having 2 doctors diagnose the PPCs independently and having a senior doctor re-inspect the results in case of inconsistencies. Finally, the fact that the present study was conducted at a single center could limit its generalizability to other populations, better randomized control trials and meta-analysis are needed to further explore the application of the MGS-2 to diagnose PPCs after OLT.

## Conclusions

Using the MGS-2 criteria help clinicians to better diagnose the PPC patients with poorer characteristics and prognosis, and to identify patients without PPCs to avoid excessive medical treatment. The MGS-2 appeared to provide more suitable and reliable criteria than the conventional broad criteria for diagnosis of PPCs in patients who had undergone OLT.

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## Conflicts of interest

None.

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