

## Predicting Delayed Ventilator Weaning after Lung Transplantation: The Role of Body Mass Index

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**Background:** Weaning from mechanical ventilation is difficult in the intensive care unit (ICU). Many controversial questions remain unanswered concerning the predictors of weaning failure. This study investigates patient characteristics and delayed weaning after lung transplantation.

**Methods:** This study retrospectively reviewed the medical records of 17 lung transplantation patients from October 2012 to December 2013. Patients able to be weaned from mechanical ventilation within 8 days after surgery were assigned to an early group (n = 9), and the rest of the patients were assigned to the delayed group (n=8). Patients' intraoperative and postoperative characteristics were collected and analyzed, and conventional weaning predictors, including rapid shallow breathing index (RSBI), were also assessed.

**Results:** The results of the early group showed a significantly shorter ICU stay in addition to a shorter hospitalization overall. Notably, the early group had a higher body mass index (BMI) than the delayed group (20.7 vs. 16.9,  $p = 0.004$ ). In addition, reopening occurred more frequently in the delayed group (1/9 vs. 5/8,  $p = 0.05$ ). During spontaneous breathing trials, tidal volume (TV) and arterial oxygen tension were significantly higher in the early group compared to the delayed weaning group, but differences in RSBI and respiratory rate (RR) between groups were not statistically significant.

**Conclusions:** Low BMI might be associated with delayed ventilator weaning in lung transplantation patients. In addition, instead of the traditional weaning predictors of RSBI and RR, TV might be a better predictor for ventilator weaning after lung transplantation.

**Key Words:** body mass index; lung transplantation; mechanical ventilation; weaning.

### Introduction

Lung transplantation is one of the few feasible treatment options for end-stage lung disease. The first lung transplantation was described in 1963,[1] and it provided decades of survival after decades.[2] Since the first successful case, the number of

transplants has continued to increase and the clinical outcomes of lung transplantation continue to improve, as the International Society of Heart and Lung Transplantation reported over 43,000 transplants worldwide, and the associated 5-year survival rate reached 53%.[3] Specifically, in Korea, the first lung transplantation was reported in 1996, and a case series of 13 patients was published in 2006.[4]

Following transplantation, the day of extubation is one of the most critical moments in the intensive care unit (ICU) stay. Early extubation after lung transplantation (within 12 hours) has been frequently reported,[5,6] but this maneuver should be performed very cautiously in select patients to avoid the serious complications associated with reintubation. The median time to extubation in lung transplantation patients was reported to be approximately 3 days, and the range was between one and 312

Received on March 26, 2014    Revised on July 27, 2014

Accepted on August 14, 2014

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\* No potential conflict of interest relevant to this article was reported.

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hours.[7,8] According to these reports, most lung transplantation patients undergo mechanical ventilator weaning and extubation while still in the ICU.

When deciding to wean patients from mechanical ventilation (MV), many parameters are considered, including demographic data, perioperative variables and laboratory data such as acceptable gas exchange. MV itself is a major determinant of ICU length of stay (LOS). One prospective study specific to lung surgery reported that preoperative body mass index (BMI) prior to lung volume reduction surgery is a sensitive measure of the patient's nutritional state, and a low BMI correlates to prolonged postoperative MV.[9] In addition to BMI, Lee et al.[10] also published that the median ICU LOS following a single lung transplantation was 5 days, and that pulmonary hypertension and poor immediate postoperative oxygenation (ratio of the partial pressure of arterial oxygen to the fraction of inspired oxygen [ $\text{PaO}_2/\text{FiO}_2$ ] of less than 200 mmHg) were good predictors of a prolonged ICU stay.[10]

Extubation and weaning from MV performed in a timely manner are critical to ICU management to reduce ICU LOS. To identify risk factors for prolonged MV after unilateral or bilateral lung transplantation, we retrospectively reviewed the medical records of lung transplantation patients who were weaned from MV. We classified and analyzed clinical data that may impact the ability to wean a patient from MV, and organized this data by the preoperative, intraoperative and postoperative periods. Lung mechanics and arterial blood gas analysis (ABGA) during spontaneous breathing trials (SBTs) were investigated, in addition to the well-known weaning predictors of tidal volume (TV), respiratory rate (RR), and rapid shallow breathing index (RSBI).[11-13]

## Materials and Methods

This retrospective study was approved by the Institutional Review Board (IRB) of Severance Hospital (Ref: 4-2013-0927), and the need for informed consent was waived by the IRB. Seventeen patients aged 18 years or older who were admitted to the ICU from October 2012 after unilateral or bilateral lung transplantation were enrolled. Exclusion criteria included early death within the immediate postoperative ICU stay and prolonged MV (> 3 months). Data were collected retrospectively by reviewing electronic medical records, and the same surgeon performed all surgeries.

Demographic data and intraoperative and postoperative variables that may impact the ability to wean a patient from MV

were investigated. Demographic data included age, gender, height, weight, BMI, and comorbid illness. Preoperative pulmonary function testing, echocardiography and 6-minute walking distance were also collected. Intraoperative variables included operation time, fluid intake, urine output, blood transfusion history, estimated blood loss, and salvaged blood from the Cell Saver (Cell Saver 5 System, Haemonetics, Braintree, MA, USA). ABGA, TV, and RR throughout the SBTs were recorded. RSBI was calculated from TV and RR.

Unless a contraindication to the SBT was present, such as acute rejection or severe bleeding, a spontaneous awakening trial (SAT) and SBT were initiated and evaluated by the multidisciplinary team, which included the surgeon, pulmonologists, anesthesiologists, pharmacists, and nurses. According to some studies, no difference in the percentage of patients passing the SBT or the percentage of patients successfully extubated between T-tube trial and low levels of pressure support (PS),[14,15] low levels of PS less than 10 cmH<sub>2</sub>O and T-tube trial were used as SBT in this study. In addition, ABGA was performed 60 minutes after the SBT. If the respiratory pattern, gas exchange, hemodynamic stability and subject comfort were sufficient to pass the SBT, extubation for endotracheally intubated patients or weaning from MV for patients with tracheostomies were done. If there was any controversy about the SBT results, the SBT was extended to 120 minutes. After a maximum duration of 120 minutes, the multidisciplinary critical care team decided whether to extubate or wean. When patients failed an initial SBT, the team reviewed possible reversible etiologies for failure, such as respiratory load (increased work of breathing, reduced compliance due to pneumonia or edema, airway difficulty), cardiac dysfunction, neuromuscular dysfunction, neuropsychological complications, metabolic disturbance, inappropriate nutrition and anemia. After correcting these etiologies, SBTs were repeated daily in order to successfully extubate the patient at the earliest possible time.

Notably, SBTs were immediately aborted in the following situations: 1. Clinical assessment and subjective indices suggesting agitation, anxiety, depressed mental status, perspiration, cyanosis, increased accessory muscle activity and dyspnea, 2. Objective measurements showing a  $\text{PaO}_2 < 60$  mmHg on  $\text{FiO}_2 \geq 0.5$  or a percutaneous oxygen saturation ( $\text{SpO}_2$ )  $\leq 88\%$ , arterial carbon dioxide partial pressures ( $\text{PaCO}_2$ )  $> 65$  mmHg, RR  $> 45$  breaths/min, RSBI  $> 105$  breaths/min/L, heart rate (HR) over 140 beats/min or sustained increase or decrease of  $> 20\%$ , systolic blood pressure (SBP)  $> 180$  mmHg or SBP  $< 90$  mmHg, and 3. Measurements showing newly developed or aggravated

cardiac arrhythmia.

Once the median duration of MV was identified, the patients were divided into two groups, either the early or delayed group, based on median duration of MV.

### Statistical analysis

Data were presented as the median (interquartile range) or the number (percentage) of patients. Data analysis was performed using the Statistical Package for the Social Sciences (SPSS, Version 18; SPSS Inc., Chicago, IL, USA). Comparisons between the two groups were analyzed using the Mann-Whitney test for continuous data and using the  $\chi^2$  test or Fisher's exact test for categorical data. A p-value less than 0.05 was considered statistically significant.

## Results

A total of 17 patients were enrolled in this study (Table 1). The median patient age was 52 years. Hospital death occurred in three patients. Etiologies of end-stage lung disease included idi-

opathic pulmonary fibrosis (9 patients), complications from bone marrow transplantation (3 patients), bronchiectasis (1 patient), usual interstitial pneumonia (1 patient), lymphangiolo-myomatosis (1 patient), dermatomyositis (1 patient) and chronic obstructive pulmonary disease (COPD) (1 patient).

In this study, the median duration of MV was 8.0 days. Brochard [16] proposed that patients who are difficult to wean often require up to three SBTs or may take as long as 7 days from the first SBT to achieve successful weaning. In our study, unless there was a contraindication to the SBT, such as acute rejection or severe bleeding, the first SBT was usually initiated the day after surgery. Therefore, patients requiring up to 7 days from the first failed SBT (post-op day 8) to achieve successful weaning were assigned to the delayed group. Thus, the early and delayed groups were defined by a MV duration of 8 days. Nine patients were classified into the early group and eight patients were classified into the delayed group. The first SBT failure rate was similar between the two groups (2/9 vs. 3/8,  $p = 0.62$ ).

In the early group, patients were older (55 vs. 48 years,  $p = 0.04$ ) and had less frequent reoperation rates (1/9 vs. 5/8,  $p =$

**Table 1.** Characteristics of patients with early and delayed weaning after lung transplantation

	Overall	Early group (n = 9)	Delayed group (n = 8)	p value
Age, yr	52 (42-58)	55 (50-65)	48 (35-53)	0.04
Sex, M	12 (70.6)	7 (77.8)	5 (62.5)	0.62
BMI, kg/m <sup>2</sup>	19.38 (16.92-20.81)	20.72 (19.13-21.94)	16.92 (13.50-19.25)	< 0.01
BSA, m <sup>2</sup>	1.55 (1.44-1.70)	1.69 (1.55-1.73)	1.49 (1.36-1.55)	0.02
KONOS registration to op., d	75 (8-256)	75 (13-295)	102 (6-211)	0.92
MV duration, d	8.0 (3.3-21.7)	3.7 (2.4-5.9)	21.7 (13.1-40.4)	< 0.01
Hospital stay, d	42.0 (27.8-71.8)	28.5 (22.5-46.3)	75.0 (43.5-122.8)	0.01
ICU stay, d	13.0 (5.5-28.5)	6.0 (5.0-8.0)	24.5 (16.0-41.8)	< 0.01
Re-open	6 (35.3)	1 (11.1)	5 (62.5)	0.05
Mortality	3 (17.6)	3 (33.3)	0 (0)	0.21
Comorbid illness				
CRF	1 (5.9)	0 (0)	1 (12.5)	0.47
Pneumonia	5 (29.4)	3 (33.3)	2 (25.0)	1.00
Long-term steroid use	11 (64.7)	6 (66.7)	5 (62.5)	0.63
Smoking	20.0 (0-30.0)	25.0 (0-32.0)	7.5 (0-28.8)	0.42
Ventilator use	6 (35.3)	3 (33.3)	3 (37.5)	0.63
ECMO use	1 (5.9)	1 (11.1)	0 (0)	1.00
Preoperative evaluation				
Six-minute walk test	195 (105-313)	280 (75-320)	140 (122-270)	0.81
FEV1 (%)	31 (21-47)	31 (23-44)	35 (18.6-41)	0.91
FVC (%)	40 (26-55)	37 (28-63)	42 (53-19)	0.95
EF (% Echo)	65 (58-69)	65 (53-70)	63 (60-67)	0.96
RVSP*, mmHg	45 (38-60)	50 (43-71)	42 (32-55)	0.25
Donor information				
Donor age, yr	40 (26-44)	40 (28-44)	40 (22-49)	0.81
Ischemic time, min	247 (176-341)	247 (229-327)	247 (147-382)	0.70

\*RVSP was measured by echocardiography or right-sided catheterization. BMI: Body Mass Index (kg/m<sup>2</sup>); BSA: Body Surface Area (m<sup>2</sup>); KONOS: Korean Network for Organ Sharing; MV: mechanical ventilation; ICU: intensive care unit; CRF: Chronic renal failure; ECMO: extracorporeal membrane oxygenation; FEV1: forced expiratory volume in 1 second; FVC: forced vital capacity; EF: ejection fraction (%); RVSP: right ventricular systolic pressure.

**Table 2.** Intraoperative variables of patients with early and delayed weaning after lung transplantation

	Overall	Early group (n = 9)	Delayed group (n = 8)	p value
Operation time, h	6.85 (6.05-8.15)	6.85 (5.43-7.40)	7.60 (6.52-9.58)	0.18
Unilateral/Bilateral	3/14	2/7	1/7	0.55
Total fluid intake, ml	8420 (5950-10400)	7820 (5250-9225)	9275 (6838-15850)	0.29
Colloid, ml	1000 (500-1500)	1000 (500-1250)	1250 (1000-1500)	0.19
pRBC, units	7 (3-13)	6 (3-9)	4 (3-16)	0.36
FFP, units	3 (1-5)	3 (2-5)	4 (1-9)	0.66
Plt conc, units	11 (6-12)	6 (3-12)	12 (6-12)	0.27
Cell saver, ml	865 (488-2583)	700 (450-1210)	2530 (500-4140)	0.14
Urine output, ml	2270 (1295-3708)	2050 (1360-3708)	2385 (1218-5145)	1.00
Blood loss, ml	2500 (2050-4500)	2500 (1925-4035)	5075 (2000-9500)	0.30
ECMO time, min	309 (256-388)	278 (231-333)	337 (282-460)	0.12

pRBC: packed red blood cells; FFP: fresh frozen plasma; Plt conc: platelet concentrate; ECMO: extracorporeal membrane oxygenation.

**Table 3.** Postoperative variables of patients with early and delayed weaning after lung transplantation

	Overall	Early group (n = 9)	Delayed group (n = 8)	p value
ECMO use (%)	8 (47.1)	1 (11.1)	7 (87.5)	< 0.01
ECMO duration, d	3 (1-9)	1	3 (1-11)	0.26
VAP (%)	7 (41.2)	1 (11.1)	6 (75.0)	0.02
Bleeding > 1000 ml/d	5 (29.4)	1 (11.1)	4 (50.0)	0.13
Arrhythmia (%)	3 (17.6)	1 (11.1)	2 (25.0)	0.58
AKI (%)	2 (11.8)	0 (0)	2 (25.0)	0.21
CRRT (%)	1 (5.9)	0 (0)	1 (12.5)	0.47
Sepsis (%)	2 (11.8)	0 (0)	2 (25.0)	0.21
Re-intubation (%)	2 (11.8)	0 (0)	2 (25.0)	0.21

ECMO: extracorporeal membrane oxygenation; VAP: ventilator associated pneumonia; AKI: acute kidney injury; CRRT: continuous renal replacement therapy.

**Table 4.** Parameters associated with the success of the first spontaneous breathing trial

	Overall	Early group (n = 9)	Delayed group (n = 8)	p value
Respiratory parameters before SBT				
TV, mL	406 (357-434)	418 (386-467)	361 (345-408)	0.043
RR (breaths/min)	16 (14-23)	16 (14-19)	23 (15-24)	0.097
RSBI (breaths/min/L)	41.7 (34.7-63.0)	36.6 (31.4-44.1)	59.5 (40.7-66.0)	0.083
Ineffective cough	12 (70.6)	6 (66.7)	6 (75.0)	1.0
Sputum > moderate	14 (82.4)	6 (66.7)	8 (100)	0.21
ABG before SBT				
pH	7.46 (7.43-7.48)	7.46 (7.44-7.47)	7.45 (7.40-7.50)	0.81
PaO <sub>2</sub>	134.6 (115.0-151.7)	145.4 (131.4-162.5)	122.8 (93.7-134.6)	0.016
PaCO <sub>2</sub>	38.3 (31.6-42.6)	41.0 (30.8-45.0)	36.8 (31.6-41.3)	0.56
PaO <sub>2</sub> /FiO <sub>2</sub>	337 (291-434)	415 (306-449)	327 (251-363)	0.10
ABG one hour after SBT				
PaO <sub>2</sub>	118.6 (98.7-147.3)	134.4 (111.0-155.1)	93.6 (80.4-129.3)	0.045
PaCO <sub>2</sub>	36.9 (31.3-47.1)	36.9 (29.1-48.4)	37.2 (34.2-46.4)	0.72
PaO <sub>2</sub> decrease (%)	13.2 (3.5-17.5)	13.2 (3.1-15.7)	13.5 (-3.4-19.8)	0.64
PaCO <sub>2</sub> decrease (%)	6.9 (-15.3-9.5)	9.0 (-14.0-15.0)	-0.1 (-28.0-10.1)	0.29
Weaning results				
First SBT-successful extubation, h	10.2 (1.9-61.1)	3.6 (1.9-21.8)	47.9 (3.9-171.9)	0.18
First SBT failure (%)	5 (29.4)	2 (22.2)	3 (37.5)	0.62
MV duration, d	8.0 (3.3-21.7)	3.7 (2.4-5.9)	21.7 (13.1-40.4)	0.001

SBT: spontaneous breathing trial; TV: tidal volume; RR: respiratory frequency; RSBI: rapid shallow breathing index (respiratory frequency to tidal volume ratio); ABG: arterial blood gas; PaO<sub>2</sub>: arterial oxygen tension; PaCO<sub>2</sub>: arterial carbon dioxide tension; MV: mechanical ventilation.

0.05) than the delayed group (Table 1). Predictably, the ICU and hospital LOS were longer in the delayed group. Also, BMI (20.7 vs. 16.9 kg/m<sup>2</sup>,  $p < 0.01$ ) and BSA (1.7 vs. 1.4 m<sup>2</sup>,  $p = 0.02$ ) were significantly higher in the early group.

Analysis of intraoperative and postoperative variables showed no significant differences between the groups, except for more frequent extracorporeal membrane oxygenation (ECMO) use and ventilator-associated pneumonia (VAP) in the delayed group (Table 2 and 3). ECMO was used when the immediate postoperative lung function was insufficient to adequately oxygenate the entire body. VAP, acute rejection and the general preoperative condition of the patient could affect postoperative lung function.

In the early group, the TV just before the SBT was significantly greater (418 vs. 361 ml,  $p = 0.04$ ) compared to the delayed group, while respiratory rate and RSBI were not significantly different between groups (Table 4). PaO<sub>2</sub> measurements prior to SBT and 1 hour after SBT were significantly higher in the early group than the delayed group, but PaO<sub>2</sub>/FiO<sub>2</sub> before SBT was not significantly different. However, patients were given different proportions of oxygen and were given oxygen via different methods after SBT. Therefore, a higher PaO<sub>2</sub> before SBT and 1 hour after SBT in the early group does not allow for conclusions to be drawn.

## Discussion

The results of the present study show that a low BMI is associated with prolonged MV after lung transplantation. In addition, larger tidal volumes before the SBT are associated with a shorter MV duration in this patient population, while the conventional weaning indicator, RSBI, did not predict early weaning from MV.

BMI and skeletal muscle mass have been reported to be good indicators of clinical outcomes in critically ill patients. In critically ill patients, the obesity-mortality paradox is a well-known phenomenon among the intensivists. In an observational study of approximately 154,000 ICU patients, BMIs less than 18.5 kg/m<sup>2</sup> demonstrated the highest mortality risk, while obese patients with BMIs ranging between 30 and 39.9 kg/m<sup>2</sup> showed the lowest risk of death (odds ratio of 0.86, 95% confidence interval 0.83-0.90).[17] In addition, Gupta et al.[18] showed that low BMIs less than 18.5 kg/m<sup>2</sup> were associated with increased mortality in 793 surgical ICU patients. Similarly, sarcopenia, based on muscle cross-sectional area at the third lumbar vertebra, was associated with fewer ventilator-free and ICU-free days in eld-

erly patients.[19] An additional retrospective investigation revealed that low BMI was associated with a higher risk of death in acute lung injury patients on MV[20], and a similar association between low BMI less than 21 and delayed weaning from MV in chronic obstructive lung disease patients has been demonstrated.[21] De la Torre et al.[22] reported that there was no correlation between low BMI and delayed weaning in patients after lung transplantation. However, their study defined low BMI to be less than 20 kg/m<sup>2</sup>, not 18.5 kg/m<sup>2</sup>, which may have blunted their effects. Because in the other study, the Toronto Lung Transplant Group revealed that lower BMI less than 17 was associated with higher risk of 90-day mortality in the patient undergoing lung transplantation.[23]

Initially, BMI measurements were introduced to be a marker of the overall nutrition status of the human body. Because adequate nutrition support can improve respiratory muscle contractility and the subsequent ability to expectorate sputum, the duration of MV in critically ill patients could be prolonged in malnourished patients. Therefore, BMI is an important reference index that can be used to estimate MV duration and predict weaning from MV for post-transplantation patients, as the results of this study have indicated.

MV weaning covers the entire process of liberating the patients from mechanical support and from the endotracheal tube. Weaning from MV starts with a clinical picture suggesting that the patient could tolerate spontaneous breathing. Then, an assessment of readiness to wean, a SBT, and extubation are carried out.[24] Previous studies have reported that the weaning failure rate after a single SBT is between 26 and 42%.[25,26]

If weaning is delayed, patients are exposed to unnecessary discomfort and the risk of complications, including stress ulcer, deep vein thrombosis or pulmonary embolism, and VAP, are increased. For these patients, the increased cost of care due to prolonged hospital and ICU stays can be devastating. The incidence of unplanned extubation ranges from 0.3 to 16%.[27] and almost half of patients who underwent unplanned extubation during the weaning period did not require reintubation.[28] These findings suggest that a significant number of critically ill patients are enduring unnecessary lengths of MV and intubation. Esteban et al.[29] demonstrated that mortality increases with increasing duration of MV, in part because of the complications of prolonged MV like VAP and airway trauma.[30] Coplin et al.[31] reported that mortality of brain-injured patients was 12% if there was no delay in extubation, but mortality was increased to 27% in cases of delayed extubation. Moreover, MV has been consistently associated with an increased cost of care of up to

US\$2,000 per day.[32] Although a relatively small percentage (6%) of ventilated patients experience prolonged MV, these patients consume 37% of ICU resources.[33] Additionally, failure to extubate is associated with high mortality and morbidity by inducing deleterious effects such as aspiration, atelectasis, and pneumonia.[34]

Patients undergoing lung transplantation should be cautiously weaned from MV in a timely manner. Most lung transplantation patients are physically debilitated because transplantation tends to be the last treatment option in end-stage lung disease. They usually suffer from long-term malnutrition and sarcopenia, lack of physical activity due to oxygenation failure, and cardiac comorbidities such as right heart failure.

In the literature, a limited number of predictors for ventilator weaning or extubation failure have been suggested.[11-13] One study reported that the immediate postoperative PaO<sub>2</sub> to FiO<sub>2</sub> ratio, a history of preexisting pulmonary hypertension, and the pulmonary blood flow distribution were good predictors of the ICU length of stay following single lung transplantation.[10] In addition to these predictors, our study suggests that preoperative BMI and larger TVs before the SBT may be reasonable predictors of weaning in lung transplantation patients. In previous literature, TV was not commonly highlighted as a predictor of delayed weaning or weaning failure. However, RSBI, which was noticed because of its high predictive value,[12] showed some trends, but the small study population may explain why RSBI failed to be a significant predictor of weaning success. Because the RR was similar between the two groups during the SBTs, RSBI was not statistically significant. The patients with end-stage lung disease had long-term exposure to hypoxia and hypercapnia, so their respiratory drive was decreased. Also, their postoperative pain was controlled with high-dose opioids, specifically remifentanyl via intravenous infusion, which may contribute to the patients breathing more deeply and slowly after lung transplantation.

In this study, older age was associated with early weaning. When we compared the younger age group (< 53 years) to the older group, the younger group also had a lower BMI. One thought is that end-stage lung disease rapidly wastes the metabolic reserve in younger patients. Total energy expenditure, which includes resting energy expenditure, is known to decrease with the aging process.[35] Therefore, it is possible that elderly patients are more resistant to malnutrition because weight-adjusted energy expenditure is lower in the elderly.[36]

Prolonged MV is associated with VAP. As demonstrated in COPD patients, higher BMIs could be associated with early

weaning from MV,[21] possibly due to improved immunity. Therefore, the relationship between BMI and VAP warrants further investigation.

Compared to other studies, the duration of MV in this study was longer, while weaning failure after the first successful SBT occurred in only two patients. These results suggest that there is room for a faster weaning process in our practice. In addition, the limited number of cases in this study requires further analysis of the variables we chose to study. The small number of the patients in this study (n = 17) is one reason why the predictive power was not analyzed by a receiver operating characteristic curve.

In the present study, we demonstrated MV more than 8 days after unilateral or bilateral lung transplantation to be associated with lower BMI and smaller tidal volume before SBT. Notably, postoperative comorbidities associated with prolonged MV were found to be ECMO use and VAP.

## References

- 1) Rutherford RM, Lordan JL, Fisher AJ, Corris PA: Historical Overview of Lung and Heart-Lung Transplantation. In: Lung and Heart-Lung Transplantation. Edited by Joseph P. Lynch III, Ross DJ: New York, Taylor and Francis Group. 2006, p 1.
- 2) Unilateral lung transplantation for pulmonary fibrosis. Toronto Lung Transplant Group. *N Engl J Med* 1986; 314: 1140-5.
- 3) Yusen RD, Christie JD, Edwards LB, Kucheryavaya AY, Benden C, Dipchand AI, et al: The Registry of the International Society for Heart and Lung Transplantation: thirtieth adult lung and heart-lung transplant report--2013; focus theme: age. *J Heart Lung Transplant* 2013; 32: 965-78.
- 4) Paik HC, Hwang JJ, Kim DH, Joung EK, Kim HK, Lee DY: The 10 years experience of lung transplantation. *Korean J Thorac Cardiovasc Surg* 2006; 39: 822-7.
- 5) Hansen LN, Ravn JB, Yndgaard S: Early extubation after single-lung transplantation: analysis of the first 106 cases. *J Cardiothorac Vasc Anesth* 2003; 17: 36-9.
- 6) Rocca GD, Coccia C, Costa GM, Pompei L, Di Marco P, Pierconti F, et al: Is very early extubation after lung transplantation feasible? *J Cardiothorac Vasc Anesth* 2003; 17: 29-35.
- 7) Low DE, Trulock EP, Kaiser LR, Pasque MK, Dresler C, Ettinger N, et al: Morbidity, mortality, and early results of single versus bilateral lung transplantation for emphysema. *J Thorac Cardiovasc Surg* 1992; 103: 1119-26.

- 8) Westerlind A, Nilsson F, Ricksten SE: The use of continuous positive airway pressure by face mask and thoracic epidural analgesia after lung transplantation. Gothenburg Lung Transplant Group. *J Cardiothorac Vasc Anesth* 1999; 13: 249-52.
- 9) Mazolewski P, Turner J, Baker M, Kurtz T, Little AG: The impact of nutritional status on the outcome of lung volume reduction surgery: a prospective study. *Chest* 1999; 116: 693-6.
- 10) Lee KH, Martich GD, Boujoukos AJ, Keenan RJ, Griffith BP: Predicting ICU length of stay following single lung transplantation. *Chest* 1996; 110: 1014-7.
- 11) Frutos-Vivar F, Ferguson ND, Esteban A, Epstein SK, Arabi Y, Apezteguía C, et al: Risk factors for extubation failure in patients following a successful spontaneous breathing trial. *Chest* 2006; 130: 1664-71.
- 12) Namen AM, Ely EW, Tatter SB, Case LD, Lucia MA, Smith A, et al: Predictors of successful extubation in neurosurgical patients. *Am J Respir Crit Care Med* 2001; 163: 658-64.
- 13) Thille AW, Cortés-Puch I, Esteban A: Weaning from the ventilator and extubation in ICU. *Curr Opin Crit Care* 2013; 19: 57-64.
- 14) Kollef MH, Shapiro SD, Silver P, St John RE, Prentice D, Sauer S, et al: A randomized, controlled trial of protocol-directed versus physician-directed weaning from mechanical ventilation. *Crit Care Med* 1997; 25: 567-74.
- 15) Matić I, Majerić-Kogler V: Comparison of pressure support and T-tube weaning from mechanical ventilation: randomized prospective study. *Croat Med J* 2004; 45: 162-6.
- 16) Brochard L: Pressure support is the preferred weaning method. As presented at the 5th International Consensus Conference in Intensive Care Medicine: Weaning from Mechanical Ventilation. Hosted by ERS, ATS, ESICM, SCCM and SRLF; Budapest, April 28-29, 2005.
- 17) Pickkers P, de Keizer N, Dusseljee J, Weerheijm D, van der Hoeven JG, Peek N: Body mass index is associated with hospital mortality in critically ill patients: an observational cohort study. *Crit Care Med* 2013; 41: 1878-83.
- 18) Gupta R, Knobel D, Gunabushanam V, Agaba E, Ritter G, Marini C, et al: The effect of low body mass index on outcome in critically ill surgical patients. *Nutr Clin Pract* 2011; 26: 593-7.
- 19) Moisey LL, Mourtzakis M, Cotton BA, Premji T, Heyland DK, Wade CE, et al: Skeletal muscle predicts ventilator-free days, ICU-free days, and mortality in elderly ICU patients. *Crit Care* 2013; 17: R206.
- 20) O'Brien JM Jr, Phillips GS, Ali NA, Lucarelli M, Marsh CB, Lemeshow S: Body mass index is independently associated with hospital mortality in mechanically ventilated adults with acute lung injury. *Crit Care Med* 2006; 34: 738-44.
- 21) Li-dong S, Chang-sheng G, Zi-yu Z: Explore the influence of BMI in the optimal time of weaning from sequential mechanical ventilation for severity chronic obstructive pulmonary disease. *BMC Emerg Med* 2013; 13(Suppl 1): S1.
- 22) de la Torre MM, Delgado M, Paradelo M, González D, Fernández R, García JA, et al: Influence of body mass index in the postoperative evolution after lung transplantation. *Transplant Proc* 2010; 42: 3026-8.
- 23) Madill J, Gutierrez C, Grossman J, Allard J, Chan C, Hutcheon M, et al: Nutritional assessment of the lung transplant patient: body mass index as a predictor of 90-day mortality following transplantation. *J Heart Lung Transplant* 2001; 20: 288-96.
- 24) Boles JM, Bion J, Connors A, Herridge M, Marsh B, Melot C, et al: Weaning from mechanical ventilation. *Eur Respir J* 2007; 29: 1033-56.
- 25) Esteban A, Alia I, Tobin MJ, Gil A, Gordo F, Vallverdú I, et al: Effect of spontaneous breathing trial duration on outcome of attempts to discontinue mechanical ventilation. Spanish Lung Failure Collaborative Group. *Am J Respir Crit Care Med* 1999; 159: 512-8.
- 26) Vallverdú I, Calaf N, Subirana M, Net A, Benito S, Mancebo J: Clinical characteristics, respiratory functional parameters, and outcome of a two-hour T-piece trial in patients weaning from mechanical ventilation. *Am J Respir Crit Care Med* 1998; 158: 1855-62.
- 27) Epstein SK: Decision to extubate. *Intensive Care Med* 2002; 28: 535-46.
- 28) Epstein SK, Nevins ML, Chung J: Effect of unplanned extubation on outcome of mechanical ventilation. *Am J Respir Crit Care Med* 2000; 161: 1912-6.
- 29) Esteban A, Anzueto A, Frutos F, Alia I, Brochard L, Stewart TE, et al: Characteristics and outcomes in adult patients receiving mechanical ventilation: a 28-day international study. *JAMA* 2002; 287: 345-55.
- 30) Tobin MJ: Mechanical ventilation. *N Engl J Med* 1994; 330: 1056-61.
- 31) Coplin WM, Pierson DJ, Cooley KD, Newell DW, Rubenfeld GD: Implications of extubation delay in brain-injured patients meeting standard weaning criteria. *Am J Respir Crit Care Med* 2000; 161: 1530-6.
- 32) Cooper LM, Linde-Zwirble WT: Medicare intensive care unit use: analysis of incidence, cost, and payment. *Crit Care*

Med 2004; 32: 2247-53.

33) Wagner DP: Economics of prolonged mechanical ventilation. *Am Rev Respir Dis* 1989; 140: S14-8.

34) Torres A, Gatell JM, Aznar E, el-Ebiary M, Puig de la Bellacasa J, González J, et al: Re-intubation increases the risk of nosocomial pneumonia in patients needing mechan-

ical ventilation. *Am J Respir Crit Care Med* 1995; 152: 137-41.

35) Roberts SB, Dallal GE: Energy requirements and aging. *Public Health Nutr* 2005; 8: 1028-36.

36) Gaillard C, Alix E, Sallé A, Berrut G, Ritz P: Energy requirements in frail elderly people: a review of the literature. *Clin Nutr* 2007; 26: 16-24.