

# Predictors of early weaning failure from mechanical ventilation in critically ill patients after emergency gastrointestinal surgery

## A retrospective study

Yun Tae Jung, MD<sup>a</sup>, Myung Jun Kim, MD<sup>b</sup>, Jae Gil Lee, MD, PhD<sup>b</sup>, Seung Hwan Lee, MD<sup>b,\*</sup>

### Abstract

Mechanical ventilation (MV) is the most common therapeutic modality used for critically ill patients. However, prolonged MV is associated with high morbidity and mortality. Therefore, it is important to avoid both premature extubation and unnecessary prolongation of MV. Although some studies have determined the predictors of early weaning success and failure, only a few have investigated these factors in critically ill surgical patients who require postoperative MV. The aim of this study was to evaluate predictors of early weaning failure from MV in critically ill patients who had undergone emergency gastrointestinal (GI) surgery.

The medical records of 3327 adult patients who underwent emergency GI surgery between January 2007 and December 2016 were reviewed retrospectively. Clinical and laboratory parameters before surgery and within 2 days postsurgery were investigated.

This study included 387 adult patients who required postoperative MV. A low platelet count (adjusted odds ratio [OR]: 0.995; 95% confidence interval [CI]: 0.991–1.000;  $P = .03$ ), an elevated delta neutrophil index (DNI; adjusted OR: 1.025; 95% CI: 1.005–1.046;  $P = .016$ ), a delayed spontaneous breathing trial (SBT; adjusted OR: 14.152; 95% CI: 6.571–30.483;  $P < .001$ ), and the presence of postoperative shock (adjusted OR: 2.436; 95% CI: 1.138–5.216;  $P = .022$ ) were shown to predict early weaning failure from MV in the study population.

Delayed SBT, a low platelet count, an elevated DNI, and the presence of postoperative shock are independent predictors of early weaning failure from MV in critically ill patients after emergency GI surgery.

**Abbreviations:** ALT = alanine transaminase, APACHE II = Acute Physiology and Chronic Health Evaluation II, AST = aspartate transaminase, ASV = adaptive support ventilation, BMI = body mass index, BUN = blood urea nitrogen, CCI = Charlson comorbidity index, CI = confidence interval, CPAP = continuous positive airway pressure, CRF = chronic renal failure, CRP = C-reactive protein, DNI = delta neutrophil index, EW = early weaning,  $\text{FIO}_2$  = fraction of inspired oxygen, GI = gastrointestinal, Hb = hemoglobin, HLOS = hospital length of stay, ICU = intensive care unit, MV = mechanical ventilation, NMB = neuromuscular blocker, OR = odds ratio, PBW = predicted body weight, PEEP = positive end expiratory pressure, PIP = peak inspiratory pressure, SAT = spontaneous awakening trial, SBT = spontaneous breathing trial, SIMV = synchronized intermittent mechanical ventilation, SOFA = sequential organ failure assessment, UTI = urinary tract infection, Vt = tidal volume, WBC = white blood cell.

**Keywords:** critically ill, mechanical ventilation, ventilator weaning

## 1. Introduction

Since its first clinical application in the 1920s, the mechanical ventilator has been continually developed and has become one of the most common therapeutic modalities used for critically ill patients in the intensive care unit (ICU).<sup>[1]</sup> The mechanical

ventilator has improved survival rates and has shortened the length of stay of patients who are unable to breathe without assistance in the ICU, by providing adequate oxygenation and ventilation until improvement in the patient's respiratory distress. To maximize the benefits of the ventilator and minimize the risk of complications in critically ill patients, it is important to avoid both premature extubation and unnecessary prolongation of MV.<sup>[2,3]</sup>

Previous studies have emphasized the importance of determining predictors of both early weaning (EW) success and EW failure.<sup>[4,5]</sup> Although some of these predictors can help intensivists to balance between deciding on EW and the appropriate lengthening of MV, only a few studies have investigated critically ill surgical patients who require the support of postoperative MV.

We designed this study to investigate the factors for EW failure from MV in critically ill patients who had undergone emergency gastrointestinal (GI) surgery.

## 2. Methods

### 2.1. Study population

The medical records of 3327 patients (older than age 18) who received emergency GI surgery for secondary peritonitis in Severance Hospital, Seoul, South Korea, from January 2007 to

Editor: Goran Augustin.

Supplemental Digital Content is available for this article.

The authors have no conflicts of interest to disclose.

<sup>a</sup>Department of Surgery, Ajou University School of Medicine, Suwon, <sup>b</sup>Division of Trauma Surgery, Department of Surgery, Yonsei University College of Medicine, Seoul, Republic of Korea.

\*Correspondence: Seung Hwan Lee, Division of Trauma Surgery, Department of Surgery, Yonsei University College of Medicine, 50-1 Yonsei-ro, Seodaemun-gu, Seoul 03722, Republic of Korea (e-mail: seunghwan@yuhs.ac).

Copyright © 2018 the Author(s). Published by Wolters Kluwer Health, Inc. This is an open access article distributed under the terms of the Creative Commons Attribution-Non Commercial License 4.0 (CCBY-NC), where it is permissible to download, share, remix, transform, and buildup the work provided it is properly cited. The work cannot be used commercially without permission from the journal.

Medicine (2018) 97:40(e12741)

Received: 14 May 2018 / Accepted: 17 September 2018

<http://dx.doi.org/10.1097/MD.00000000000012741>

December 2016, were reviewed, retrospectively. Emergency GI surgery included surgeries performed within 12 hours after the diagnosis. The study was approved by the Institutional Review Board of Severance Hospital, Yonsei University Health System (4-2017-0420); informed consent was waived because of the retrospective nature of the study.

Of 3327 patients, 1926 patients who received emergency surgery for acute appendicitis were excluded. Among 1401 patients who underwent emergency GI surgery for diffuse peritonitis, we also excluded patients (n=1014) who were extubated or weaned from MV immediately after surgery. Patients with diffuse peritonitis due to GI perforation, intestinal strangulation with ischemia, and acute mesenteric ischemia were included. Finally, 387 critically ill patients who maintained endotracheal intubation and MV after emergency GI surgery for diffuse peritonitis were selected for analysis. The patients were divided into 2 groups according to the duration of MV. Patients who were extubated and weaned from MV within 48 hours postsurgery were included in the EW success group, and the remainder of the patients who had failed EW were included in the EW failure group (Fig. 1).

## 2.2. Data collection and definition

Baseline characteristics of each patient including age, sex, and medical history were obtained. Perioperative clinical data, surgery-related variables, laboratory results immediately after surgery, parameters from the mechanical ventilator, and the clinical outcome of each patient were also collected from electronic medical records. The laboratory variables were measured immediately after surgery.

Shock was defined as a systolic blood pressure of less than 90 mm Hg despite adequate fluid resuscitation or the need for a vasopressor (norepinephrine and/or vasopressin) to maintain a mean arterial pressure of greater than 65 mm Hg within 24 hours preoperatively (preoperative shock) or 24 hours postoperatively (postoperative shock).

Intraoperative fluid intake and output and fluid intake and output within 48 hours after surgery were calculated and presented as the cumulative fluid intake. The proportion of patients with positive cumulative fluid balance was determined.

The spontaneous awakening trial (SAT) was performed for each patient who passed the screening process. Patients passed the safety screening when they met the following criteria: not receiving a sedative infusion for active seizures or alcohol withdrawal, not receiving increasing sedative doses because of ongoing agitation, not receiving neuromuscular blockers (NMBs), no evidence of active myocardial ischemia within 24 hours, and no evidence of increased intracranial pressure.<sup>[6]</sup> SAT involved an attempt on the discontinuation or cessation of all intravenous sedatives, and awakening efforts were carried out by an intensivist. The spontaneous breathing trial (SBT) was performed on patients who passed SAT and SBT safety screenings, and the process included switching the ventilator mode from the mandatory ventilation mode to pressure support ventilation or continuous positive airway pressure, allowing patients' own breathing efforts for a period of 30 minutes to 2 hours. SBT safety screening had the following criteria: adequate oxygenation, spontaneous inspiratory effort, and no significant use of vasopressors or inotropes.<sup>[6]</sup>

## 2.3. Statistical analysis

Before statistical analysis, data normality was tested using the Shapiro–Wilk test. Continuous variables are expressed as means  $\pm$  standard deviations or as medians (the 25th and 75th quantiles) depending on the data distribution and were evaluated using the Student *t* test or Mann–Whitney *U* test, as appropriate. Categorical variables are expressed as numbers (%) and were evaluated using the Chi-square test or Fisher exact test, as appropriate. To determine risk factors for EW failure, multivariate logistic regression analysis was performed using the maximum likelihood method and backward stepwise selection. Goodness-of-fit was assessed using the Hosmer–Lemeshow test.

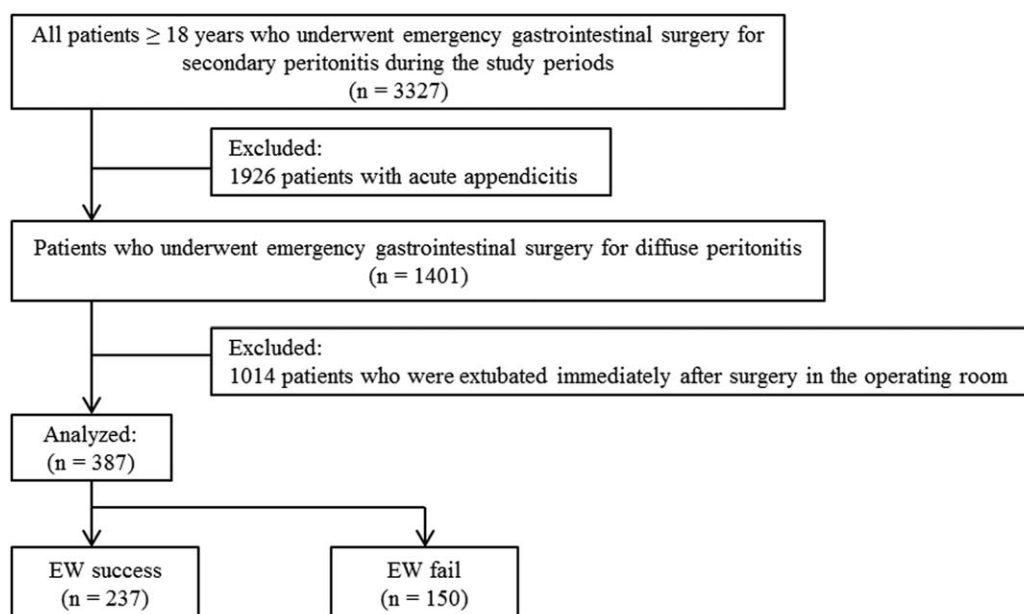


Figure 1. Flow diagram of patients selected for analysis.

Findings were considered statistically significant at  $P$  values  $<.05$ . Odds ratios (ORs) were calculated from the coefficients in the logistic regression model and 95% confidence intervals (CIs) were calculated for all variables. Statistical analysis was performed using SPSS Statistics 23.0 (IBM Corp., Armonk, NY).

### 3. Results

#### 3.1. Baseline characteristics of patients

Among the 387 patients who required postoperative MV therapy, 237 (61.2%) patients succeeded on EW, while 150 (38.8%) patients did not. The median age of the patients was 65 years in the EW success group and 69 years in the EW failure group ( $P=.054$ ). A higher proportion of men was noted in the EW failure group than in the EW success group (70.7% vs 57.8%;  $P=.011$ ). The American Society of Anesthesiologists score [3.0 (2.0, 4.0) vs 2.0 (1.0, 3.0);  $P=.003$ ], acute physiology and chronic health evaluation II score [27.0 (21.0, 33.0) vs 25.0 (18.3, 30.0);  $P=.004$ ], and quick sequential organ failure assessment (qSOFA) score [1.0 (0, 1.0) vs 0 (0, 1.0);  $P<.001$ ] were higher in the EW failure group than in the EW success group but Carlson

comorbidity index [5.0 (3.0, 6.0) vs 5.0 (3.0, 6.0);  $P=.295$ ] showed no significant difference between the 2 groups (Table 1).

#### 3.2. Clinical outcomes

Ventilator-free days [27.0 (27.0, 27.0) vs 18.0 (5.0, 23.3) days;  $P<.001$ ] and ICU-free days [26.0 (24.0, 26.0) vs 13.5 (0, 21.0) days;  $P<.001$ ] were higher in the EW success group. Hospital length of stay [21.0 (14.0, 37.0) vs 28.0 (16.0, 47.5) days;  $P=.003$ ] was shorter in the EW success group. In-hospital mortality rate was higher in the EW failure group (39.3 vs 13.5%;  $P<.001$ ) than in the EW success group (Table 1).

#### 3.3. Perioperative clinical variables

Perforation was the most common cause for emergency GI surgery, followed by strangulation and ischemia. The colon and rectum were the most commonly involved sites. Many cases involved open surgery; laparoscopic surgeries were performed in less than 10% of the patients. In the EW failure group, more patients had preoperative shock (47.3% vs 27.0%;  $P<.001$ ), postoperative shock (68.0% vs 39.7%;  $P<.001$ ), and

**Table 1**

**Baseline characteristics of the study population.**

Characteristics	EW success (n=237)	EW fail (n=150)	P
Age, median (Q1, Q3), y	65 (54.0, 76.5)	69 (58.0, 76.0)	.054*
Sex, M/F, n (%)	137 (57.8)/100 (42.2)	106 (70.7)/44 (29.3)	.011
Body weight, median (Q1, Q3), kg	57.3 (50.0, 66.0)	60 (51.9, 67.0)	.117*
BMI, median (Q1, Q3), kg/m <sup>2</sup>	21.8 (19.8, 24.5)	22.1 (20.2, 24.6)	.338*
ASA score, median (Q1, Q3)	2.0 (1.0, 3.0)	3.0 (2.0, 4.0)	.003*
APACHE II score, median (Q1, Q3)	25.0 (18.3, 30.0)	27.0 (21.0, 33.0)	.004*
qSOFA score, median (Q1, Q3)	0 (0, 1.0)	1.0 (0, 1.0)	<.001*
CCI, median (Q1, Q3)	5.0 (3.0, 6.0)	5.0 (3.0, 6.0)	.295*
Comorbidity, n (%)			
Hypertension	105 (44.3)	74 (49.3)	.334
Diabetes	45 (19.0)	36 (24.0)	.238
CRF	19 (8.0)	19 (12.7)	.134
Pulmonary diseases	72 (30.4)	56 (37.3)	.065
Malignancy	124 (52.3)	66 (44.0)	.111
Diagnosis, n (%)			.592
Perforation	194 (81.9)	121 (80.7)	
Strangulation	30 (12.7)	17 (11.3)	
Ischemia	13 (5.5)	12 (8.0)	
Perforation site, n (%)			.807
Stomach	41 (17.3)	23 (15.3)	
Small bowel	72 (30.4)	52 (34.7)	
Colorectal	93 (39.2)	58 (38.7)	
Laparoscopy/open, n (%)	22 (9.3)/215 (90.7)	5 (3.3)/145 (96.7)	.025
Preoperative shock, n (%)	64 (27.0)	71 (47.3)	<.001
Postoperative shock, n (%)	94 (39.7)	102 (68.0)	<.001
Postoperative AF, n (%)	26 (11.0)	36 (24.0)	.001
Perioperative pneumonia, n (%)	31 (13.1)	34 (22.7)	.014
Perioperative UTI, n (%)	78 (32.9)	40 (26.7)	.194
Cumulative fluid intake, median (Q1, Q3), mL	3445.0 (2266.0, 5401.0)	5130.0 (3262.0, 7648.0)	<.001*
Positive cumulative fluid balance, n (%)	226 (95.4)	147 (98.0)	.264†
HLOS, median (Q1, Q3), d	21.0 (14.0, 37.0)	28.0 (16.0, 47.5)	.003*
ICU-free days, median (Q1, Q3), d	26.0 (24.0, 26.0)	13.5 (0.0, 21.0)	<.001*
Ventilator-free days, median (Q1, Q3), d	27.0 (27.0, 27.0)	18.0 (5.0, 23.3)	<.001*
In hospital mortality, n (%)	32 (13.5)	59 (39.3)	<.001

AF = Atrial fibrillation, APACHE II = acute physiology and chronic health evaluation II, ASA = American Society of Anesthesiologists, BMI = body mass index, CCI = Charlson comorbidity index, CRF = chronic renal failure, EW = early weaning, HLOS = hospital length of stay, ICU = intensive care unit, Q1 = the 25th quantile, Q3 = the 75th quantile, qSOFA = quick sequential organ failure assessment, UTI = urinary tract infection.

\* Results from Mann-Whitney  $U$  test.

† The result from Fisher exact test.

**Table 2****Mechanical ventilator-related variables immediately after surgery.**

Ventilator parameters	EW success (n=237)	EW fail (n=150)	P
Ventilator mode, n (%)			.009*
Volume control	116 (48.9)	80 (53.3)	
Pressure control	19 (8.0)	26 (17.3)	
SIMV	88 (37.1)	37 (24.7)	
ASV	6 (2.5)	1 (0.7)	
CPAP	8 (3.4)	6 (4.0)	
FiO <sub>2</sub> , median (Q1, Q3)	0.4 (0.4, 0.4)	0.4 (0.4, 0.5)	<.001 <sup>†</sup>
V <sub>t</sub> , median (Q1, Q3), mL	400.0 (350.0, 450.0)	400.0 (350.0, 450.0)	.215 <sup>†</sup>
V <sub>t</sub> /PBW, median (Q1, Q3), mL/kg	6.7 (6.0, 7.8)	6.8 (6.1, 7.9)	.667 <sup>†</sup>
PIP, median (Q1, Q3), cmH <sub>2</sub> O	16.0 (14.0, 18.3)	17.0 (13.0, 20.5)	.023 <sup>†</sup>
PEEP, median (Q1, Q3), cmH <sub>2</sub> O	5.0 (5.0, 5.0)	5.0 (5.0, 6.0)	<.001 <sup>†</sup>
Sedatives, n (%)			<.001*
Midazolam	42 (17.7)	39 (26.0)	
Ketamine	23 (9.7)	36 (24.0)	
Propofol	134 (56.5)	62 (41.3)	
Dexmedetomidine	2 (0.8)	3 (2.0)	
Fentanyl	36 (15.2)	10 (6.7)	
Neuromuscular blockade, n (%)	1 (0.4)	13 (8.7)	<.001*
Delayed SAT, n (%)	10 (4.2)	63 (42.0)	<.001
Delayed SBT, n (%)	22 (9.3)	108 (72.0)	<.001

ASV = adaptive support ventilation, CPAP = continuous positive airway pressure, EW = early weaning, FiO<sub>2</sub> = fraction of inspired oxygen, PBW = predicted body weight, PEEP = positive end expiratory pressure, PIP = peak inspiratory pressure, Q1 = the 25th quantile, Q3 = the 75th quantile, SAT = spontaneous awakening trial, SBT = spontaneous breathing trial, SIMV = synchronized intermittent mechanical ventilation, V<sub>t</sub> = tidal volume.

\* Results from Fisher exact test.

<sup>†</sup> Results from Mann–Whitney U test.

postoperative atrial fibrillation (24.0% vs 11.0%;  $P = .001$ ) than in the EW success group. More patients who experienced failed EW had perioperative pneumonia (22.7% vs 13.1%;  $P = .014$ ), but the proportion of patients who had perioperative urinary tract infection (26.7% vs 32.9%;  $P = .194$ ) was not significantly different between the groups. The EW failure group had a higher cumulative fluid intake [5130.0 (3262.0, 7648.0) vs 3445.0 (2266.0, 5401.0) mL;  $P < .001$ ], but the proportion of patients with a positive cumulative fluid balance (98.0% vs 95.4%;  $P = .264$ ) was not significantly different (Table 1).

### 3.4. Mechanical ventilator parameters and sedatives

Patients who experienced failed EW were more frequently treated with the volume control and pressure control modes than those who had EW success (70.6% vs 56.9%;  $P = .009$ ). The EW success group had a significantly lower fraction of inspired oxygen [FiO<sub>2</sub>; 0.4 (0.4, 0.4) vs 0.4 (0.4, 0.5);  $P < .001$ ], peak inspiratory pressure [PIP; 16.0 (14.0, 18.3) vs 17.0 (13.0, 20.5) cmH<sub>2</sub>O;  $P = .023$ ], and positive end expiratory pressure [PEEP; 5.0 (5.0, 5.0) vs 5.0 (5.0, 6.0) cmH<sub>2</sub>O;  $P < .001$ ] than the EW failure group. Longer-acting sedatives were used in patients who had failed EW ( $P < .001$ ) than in those who experienced success. More patients in the EW failure group received NMBs (8.7% vs 0.4%;  $P < .001$ ) than those in the EW success group. SAT (42.0% vs 4.2%;  $P < .001$ ) and SBT (72.0% vs 9.3%;  $P < .001$ ) were delayed more often in the EW failure group than in the EW success group because more patients in this group dropped out from the early screening process within 24 hours postsurgery (Table 2).

### 3.5. Immediate postoperative laboratory variables

The EW failure group had a significantly higher delta neutrophil index [DNI; 21.3 (5.2, 42.2) vs 6.9 (3.1, 17.6) %;  $P < .001$ ],

blood urea nitrogen [26.6 (16.8, 38.4) vs 18.9 (12.1, 28.6) mg/dL;  $P < .001$ ], creatinine [1.3 (0.8, 2.0) vs 0.9 (0.6, 1.4) mg/dL;  $P < .001$ ], phosphorus [3.7 (3.0, 5.0) vs 3.3 (2.5, 4.2) mg/dL;  $P < .001$ ], and lactate [2.5 (1.6, 3.9) vs 1.7 (1.0, 2.7) mmol/L;  $P < .001$ ] and a significantly lower platelet count [120.0 (79.8, 197.3) vs 179.0 (122.0, 249.5)  $\times 10^3/\mu\text{L}$ ;  $P < .001$ ] and base excess ( $-5.08 \pm 4.35$  vs  $-4.18 \pm 3.63$ ;  $P = .039$ ) than the EW success group (Table 3). We also analyzed the association between elevated DNI and clinical outcomes, such as in-hospital mortality and hospital stay (see Table, Supplemental Digital Content 1, which illustrates an association between delta-neutrophil index and clinical outcomes, <http://links.lww.com/MD/C542>).

### 3.6. Multivariate logistic regression analysis

Multivariate logistic regression analysis revealed that a delayed SBT [adjusted OR: 14.152 (6.571–30.483);  $P < .001$ ] due to drop out from SAT or the early SBT screening within 24 hours after surgery, an elevated DNI [adjusted OR: 1.025 (1.005–1.046);  $P = .016$ ], low platelet count [adjusted OR: 0.995 (0.991–1.000);  $P = .030$ ], and the presence of postoperative shock [adjusted OR: 2.436 (1.138–5.216);  $P = .022$ ] were associated with a higher risk of EW failure (Table 4).

## 4. Discussion

Prolonged MV and premature weaning followed by reintubation are associated with higher mortality and morbidity in critically ill patients.<sup>[2,3,7,8]</sup> Precise weaning strategies to enable EW success are currently being researched by many investigators. The results of our study suggest that a delayed SBT due to drop out from SAT or the early SBT screening process within 24 hours postsurgery, an elevated DNI, a low platelet count, and the presence of postoperative shock were independent predictors of EW failure.



**Table 3**  
**Immediate postoperative laboratory results.**

Laboratory values	EW success (n=237)	EW fail (n=150)	P
Hb, median (Q1, Q3), g/dL	9.8 (8.8, 11.2)	9.8 (8.8, 11.3)	.907*
WBC, median (Q1, Q3), 10 <sup>3</sup> /uL	9.5 (6.3, 14.6)	9.2 (5.2, 15.2)	.713*
DNI, median (Q1, Q3), %	6.9 (3.1, 17.6)	21.3 (5.2, 42.2)	<.001*
Platelet, median (Q1, Q3), 10 <sup>3</sup> /uL	179.0 (122.0, 249.5)	120.0 (79.8, 197.3)	<.001*
CRP, median (Q1, Q3), mg/L	167.3 (96.6, 239.0)	159.1 (73.9, 255.9)	.876*
Base excess, mmol/L	-4.18±3.63	-5.08±4.35	.039*
Lactate, median (Q1, Q3), mmol/L	1.7 (1.0, 2.7)	2.5 (1.6, 3.9)	<.001*
BUN, median (Q1, Q3), mg/dL	18.9 (12.1, 28.6)	26.6 (16.8, 38.4)	<.001*
Creatinine, median (Q1, Q3), mg/dL	0.9 (0.6, 1.4)	1.3 (0.8, 2.0)	<.001*
Calcium	7.6 (7.2, 8.1)	7.5 (7.1, 8.0)	.052*
Phosphorus	3.3 (2.5, 4.2)	3.7 (3.0, 5.0)	<.001*

ALT=alanine transaminase, AST=aspartate transaminase, BUN=blood urea nitrogen, CRP=c-reactive protein, DNI=delta neutrophil index, EW=early weaning, Hb=hemoglobin, Q1=the 25th quantile, Q3=the 75th quantile, WBC=white blood cell.

\*Results from Mann-Whitney U test.

Patients are generally weaned from MV after SBT when they met the following criteria: resolution or stabilization of the underlying disease; adequate gas exchange; hemodynamic stability, and capacity to breathe spontaneously.<sup>[9-11]</sup> Previous studies showed that early SAT and SBT aided EW, resulting in reduced duration of MV.<sup>[6,12]</sup> Current guidelines proposed by The American College of Critical Care Medicine recommend daily sedative interruption and spontaneous breathing trials.<sup>[11]</sup> Furthermore, delayed initiation of SBT due to drop out from SAT or the early SBT screening process within 24 hours postsurgery was shown to affect MV duration in our study.

Among the laboratory results obtained immediately after surgery, DNI and platelet count showed significant differences between the 2 groups. A low platelet count is highly associated with organ dysfunction as it is a component of the SOFA score; this may delay the weaning of patients.<sup>[13-15]</sup> Organ dysfunction should be resolved for easy and successful weaning from MV. Another important laboratory parameter, DNI, reflects the activation of the immune system by showing the fraction of circulating immature granulocytes. Many investigators have reported DNI to be a useful marker for predicting the severity and prognosis of many infectious diseases.<sup>[16-19]</sup> Our study showed an association between an elevated DNI and a longer MV duration. Furthermore, elevated DNI was associated with a higher in-hospital mortality rate and a longer ICU stay. In our study population, many patients had a higher DNI level in the postoperative period than in the preoperative period. This could be possibly explained by the presence of inflammation due to the GI surgery. Additional investigations should be performed to explain this phenomenon clearly.

Sepsis/septic shock is one of the main causes of mortality and morbidity after emergent GI surgery.<sup>[20]</sup> Patients with perioperative shock were more significantly associated with EW failure in our

study. This finding is consistent with that of a report in which patients with sepsis and septic shock had a higher respiratory rate/tidal volume ratio and lower maximal inspiratory pressure and were more likely to have failed EW.<sup>[21]</sup> Patients with hemodynamic instability are not indicated for weaning from MV. Moreover, in our study, postoperative shock, not preoperative shock, was clearly associated with a longer MV duration.

Fluid therapy is an essential treatment for patients with septic and other critical conditions. Although it is difficult to define the optimal fluid balance, in some previous studies, a higher cumulative fluid intake after ICU admission was associated with higher mortality and morbidity, such as acute kidney injury.<sup>[22-24]</sup> Our study revealed that a higher cumulative fluid intake also affects MV duration. Although the cumulative fluid intake was not associated with EW failure, we can assume that the fluid status of an individual is important in the weaning process. Another factor that could prolong MV duration is atrial fibrillation. Tseng et al<sup>[25]</sup> and Marcelino et al<sup>[26]</sup> showed that atrial fibrillation in patients on ICU admission was an independent risk factor for weaning failure, as well as for poor hospital outcomes.

A low tidal volume strategy is reported to be beneficial for critically ill patients in many studies,<sup>[27,28]</sup> as it reduces mechanical ventilator-associated complications.<sup>[29]</sup> In our study, both groups had an average tidal volume of 6 to 8 mL/kg; this reflects that low tidal volume ventilation was well maintained. The EW failure group had a significantly higher initial FiO<sub>2</sub>, PIP, and PEEP, but the average of these values in both groups were within the weaning criteria range.

Because of these possible causes, none of the ventilator settings was identified as a predictor of EW failure; however, careful interpretation of the results is required and individualization of the treatment and planning is necessary.

Sedatives were used differently in the 2 groups. Longer-acting sedatives were used more frequently in the EW failure group. Recent studies have reported that short-acting sedatives reduce MV duration.<sup>[30-32]</sup> Thus, evidence from both this study and previous reports indicates that light to moderate sedation with short-acting sedatives is the recommended strategy.<sup>[33]</sup> In addition, although the EW failure group had a significantly higher frequency of NMB use than the EW success group in the univariate analysis, multivariate logistic regression analysis revealed that NMBs were not associated with EW failure. Therefore, our results should be carefully interpreted and strictly applied to a wider context involving patients' clinical condition, clinical setting, and many other factors associated with individuals.

**Table 4**  
**Multivariable logistic regression analysis of predictors for early weaning failure.**

Variables	Adjusted OR	95% CI	P
Postoperative shock	2.436	1.138-5.216	.022
Delayed SBT	14.152	6.571-30.483	<.001
DNI	1.025	1.005-1.046	.016
Platelet	0.995	0.991-1.000	.030

CI=confidence interval, DNI=delta neutrophil index, OR=odds ratio, SBT=spontaneous breathing trial.

There are several limitations to this study. First, this was a single center study with a small sample population. Second, the retrospective design involving medical record review was a weak point. Despite its importance, plateau pressure data were missing for many patients. Thus, these data were not included in the analysis. Third, changes in ventilator settings and laboratory values during the postoperative treatment period were not reflected in the study data. To identify immediate postoperative patients at risk of prolonged MV, only preoperative and immediate postoperative statuses were included in the analysis. Fourth, despite its importance,

## 5. Conclusion

Delayed initiation of SBT, an elevated DNI, a low platelet count, and the presence of postoperative shock were independent predictors of EW failure from MV in critically ill patients after emergency GI surgery. These values can be helpful in making precise decisions on weaning timing and strategy.

## Acknowledgments

The authors would like to thank JE Moon and HY Kim for assisting with the statistical analyses, and we thank all the coordinators for their valuable help and cooperation.

## Author contributions

**Conceptualization:** Jae Gil Lee, Seung Hwan Lee.

**Data curation:** Yun Tae Jung, Seung Hwan Lee.

**Formal analysis:** Yun Tae Jung, Seung Hwan Lee.

**Methodology:** Yun Tae Jung, Myung Jun Kim, Jae Gil Lee, Seung Hwan Lee.

**Writing—original draft:** Yun Tae Jung.

**Writing—review & editing:** Yun Tae Jung, Myung Jun Kim, Jae Gil Lee, Seung Hwan Lee.

## References

- [1] Slutsky AS. Mechanical ventilation. American College of Chest Physicians' Consensus Conference. *Chest* 1993;104:1833–59.
- [2] Thille AW, Harrois A, Schortgen F, et al. Outcomes of extubation failure in medical intensive care unit patients. *Crit Care Med* 2011;39:2612–8.
- [3] Penuelas O, Frutos-Vivar F, Fernandez C, et al. Characteristics and outcomes of ventilated patients according to time to liberation from mechanical ventilation. *Am J Respir Crit Care Med* 2011;184:430–7.
- [4] Meade M, Guyatt G, Cook D, et al. Predicting success in weaning from mechanical ventilation. *Chest* 2001;120:400s–24s.
- [5] Seymour CW, Martinez A, Christie JD, et al. The outcome of extubation failure in a community hospital intensive care unit: a cohort study. *Crit Care* 2004;8:R322–7.
- [6] Girard TD, Kress JP, Fuchs BD, et al. Efficacy and safety of a paired sedation and ventilator weaning protocol for mechanically ventilated patients in intensive care (Awakening and Breathing Controlled trial): a randomised controlled trial. *Lancet* 2008;371:126–34.
- [7] Epstein SK, Ciubotaru RL, Wong JB. Effect of failed extubation on the outcome of mechanical ventilation. *Chest* 1997;112:186–92.
- [8] Demling RH, Read T, Lind LJ, et al. Incidence and morbidity of extubation failure in surgical intensive care patients. *Crit Care Med* 1988;16:573–7.
- [9] MacIntyre N. Discontinuing mechanical ventilatory support. *Chest* 2007;132:1049–56.
- [10] Eskandar N, Apostolakis MJ. Weaning from mechanical ventilation. *Crit Care Clin* 2007;23:263–74. x.
- [11] Barr J, Fraser GL, Puntillo K, et al. Clinical practice guidelines for the management of pain, agitation, and delirium in adult patients in the intensive care unit. *Crit Care Med* 2013;41:263–306.
- [12] Ely EW, Baker AM, Dunagan DP, et al. Effect on the duration of mechanical ventilation of identifying patients capable of breathing spontaneously. *N Engl J Med* 1996;335:1864–9.
- [13] Rhodes A, Evans LE, Alhazzani W, et al. Surviving sepsis campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016. *Crit Care Med* 2017;45:486–552.
- [14] Perez-Fernandez X, Sabater-Riera J, Sileanu FE, et al. Clinical variables associated with poor outcome from sepsis-associated acute kidney injury and the relationship with timing of initiation of renal replacement therapy. *J Crit Care* 2017;40:154–60.
- [15] Middleton E, Rondina MT. Platelets in infectious disease. *Hematology Am Soc Hematol Educ Program* 2016;2016:256–61.
- [16] Seok Y, Choi JR, Kim J, et al. Delta neutrophil index: a promising diagnostic and prognostic marker for sepsis. *Shock* 2012;37:242–6.
- [17] Kim H, Kong T, Chung SP, et al. Usefulness of the delta neutrophil index as a promising prognostic marker of acute cholangitis in emergency departments. *Shock* 2017;47:303–12.
- [18] Shin DH, Cho YS, Kim YS, et al. Delta neutrophil index: a reliable marker to differentiate perforated appendicitis from non-perforated appendicitis in the elderly. *J Clin Lab Anal* 2017;doi:10.1002/jcla.22177.
- [19] Park BH, Kang YA, Park MS, et al. Delta neutrophil index as an early marker of disease severity in critically ill patients with sepsis. *BMC Infect Dis* 2011;11:299.
- [20] Fried E, Weissman C, Sprung C. Postoperative sepsis. *Curr Opin Crit Care* 2011;17:396–401.
- [21] Amoateng-Adjepong Y, Jacob BK, Ahmad M, et al. The effect of sepsis on breathing pattern and weaning outcomes in patients recovering from respiratory failure. *Chest* 1997;112:472–7.
- [22] Sakr Y, Rubatto Birri PN, Kotfis K, et al. Higher fluid balance increases the risk of death from sepsis: results from a large international audit. *Crit Care Med* 2017;45:386–94.
- [23] Acheampong A, Vincent JL. A positive fluid balance is an independent prognostic factor in patients with sepsis. *Crit Care* 2015;19:251.
- [24] de Oliveira FS, Freitas FG, Ferreira EM, et al. Positive fluid balance as a prognostic factor for mortality and acute kidney injury in severe sepsis and septic shock. *J Crit Care* 2015;30:97–101.
- [25] Tseng YH, Ko HK, Tseng YC, et al. Atrial fibrillation on intensive care unit admission independently increases the risk of weaning failure in nonheart failure mechanically ventilated patients in a medical intensive care unit: a retrospective case-control study. *Medicine (Baltimore)* 2016;95:e3744.
- [26] Marcelino P, Germano N, Nunes AP, et al. [Cardiac influence on mechanical ventilation time and mortality in exacerbated chronic respiratory failure patients. The role of echocardiographic parameters]. *Rev Port Pneumol* 2006;12:131–46.
- [27] Neto AS, Simonis FD, Barbas CS, et al. Lung-protective ventilation with low tidal volumes and the occurrence of pulmonary complications in patients without acute respiratory distress syndrome: a systematic review and individual patient data analysis. *Crit Care Med* 2015;43:2155–63.
- [28] Brower RG, Matthay MA, Morris A, et al. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. *N Engl J Med* 2000;342:1301–8.
- [29] Determann RM, Royakkers A, Wolthuis EK, et al. Ventilation with lower tidal volumes as compared with conventional tidal volumes for patients without acute lung injury: a preventive randomized controlled trial. *Crit Care* 2010;14:R1.
- [30] Mogahd MM, Mahran MS, Elbaradi GF. Safety and efficacy of ketamine-dexmedetomidine versus ketamine-propofol combinations for sedation in patients after coronary artery bypass graft surgery. *Ann Card Anaesth* 2017;20:182–7.
- [31] Constantin JM, Momon A, Mantz J, et al. Efficacy and safety of sedation with dexmedetomidine in critical care patients: a meta-analysis of randomized controlled trials. *Anaesth Crit Care Pain Med* 2016;35:7–15.
- [32] Fraser GL, Devlin JW, Worby CP, et al. Benzodiazepine versus nonbenzodiazepine-based sedation for mechanically ventilated, critically ill adults: a systematic review and meta-analysis of randomized trials. *Crit Care Med* 2013;41:S30–8.
- [33] Jakob SM, Ruokonen E, Grounds RM, et al. Dexmedetomidine vs midazolam or propofol for sedation during prolonged mechanical ventilation: two randomized controlled trials. *JAMA* 2012;307:1151–60.