Observational Study

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Predictors of prolonged mechanical ventilation identified at an emergency visit for elderly people

A retrospective cohort study

Hideki Mori, MD[a,*], Kazumi Yamasaki, MD, PhD[b], Takehiro Itoh, RN, NP, MSN[c], Yusuke Saishoji, MD[a], Yuichi Torisu, MD[a], Takahiro Mori, MD[a], Yasumori Izumi, MD, PhD[a]

Abstract

The aim of this study was to determine the factors that are associated with prolonged mechanical ventilation in elderly patients.

Retrospective cohort study

Single tertiary hospital in Japan

We retrospectively identified 228 patients aged 75 years or older who were admitted to a single tertiary care center in Japan between January 1, 2014 and December 31, 2017 because of endogenous diseases and underwent mechanical ventilation.

The primary outcome was extubation difficulty, which was defined as the need for mechanical ventilation for more than 14 days after intubation, reintubation within 72 hours after extubation, tracheotomy or extubation, or death within 14 days after intubation.

A multivariate analysis showed that age (odds ratio [OR] = 0.95; 95% confidence interval [CI] = 0.66–1.38; $P = .80$), gender (OR = 0.56; 95%CI = 0.27–1.17; $P = .13$), body mass index (BMI) (OR = 1.05; 95%CI = 0.98–1.14; $P = .16$), smoking history (OR = 0.64; 95%CI = 0.29–1.41; $P = .27$), Activities of daily living (ADL) (OR = 0.95; 95%CI = 0.49–1.83; $P = .87$), and modified acute physiology and chronic health evaluation (APACHE) II score (OR = 1.02; 95%CI = 0.95–1.09; $P = .61$) were not statistically significantly different. However, there were statistically significant differences in extubation difficulty between patients with diabetes mellitus (OR = 2.3; 95% CI = 1.01–5.12; $P = .04$) and those with cardiovascular disease diagnosis on admission (OR = 0.31; 95%CI = 0.1–0.97; $P = .04$).

Diabetes mellitus and cardiovascular disease diagnosis on admission were factors that were associated with prolonged mechanical ventilation in the elderly. The results of this study may help to support shared decision making with patients or surrogate decision makers at the start of intensive care in the elderly.

Abbreviations: ADL = activities of daily living, APACHE = acute physiology and chronic health evaluation, ARDS = acute respiratory distress syndrome, BMI = body mass index, CI = confidence interval, GFR = glomerular filtration rate, OR = odds ratio, ICD-10 = the International Statistical Classification of Diseases and Related Health Problems 10th Revision.

Keywords: aged, intensive care, prolonged mechanical ventilation

1. Introduction

Along with the increase in the elderly population, emergency transportation of elderly people has increased, and the number of elderly people who need intensive care has also increased.[1] There are various discussions about intensive care for the elderly.[2,3] It has been reported that there is no difference in prognosis between older and younger patients[4] and that total hospitalization costs are also lower in older patients.[5] Additionally, intensive care should not be withheld only based on chronological age as a factor.[6,7] However, for starting ventilator management, deterioration of the life prognosis, deterioration of the quality of life, increased health care expenses, and an increased care burden were reported to occur if there is difficulty extubating the patient and prolonged ventilator management is required; thus, careful judgment is required.[8–13] Previous studies showed the relevance of clinical data after beginning mechanical ventilation management compared with the outcomes of prognosis and ventilation withdrawal,[14,15] but few reports have clarified the relationship between patient factors that are found early during emergency admission and extubation difficulty. When starting intensive care for the elderly, it is important to be able to provide decision support and information as accurately as possible before starting mechanical ventilation management to decide whether or not to start long-term

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[a] Department of General Internal Medicine, [b] Clinical Research Center, [c] Nursing Department, National Hospital Organization, Nagasaki Medical Center, 2-1001-1 Kubara, Omura, Nagasaki, Japan.

[*] Correspondence: Hideki Mori, Department of General Internal Medicine, National Hospital Organization, Nagasaki Medical Center, 2-1001-1 Kubara, Omura 856-8562, Nagasaki, Japan (e-mail: mori.hideki.fu@mail.hosp.go.jp).

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ventilator management. The purpose of this study is to clarify the relationship between the factors that are identified at the emergency consultation early stage and extubation difficulty in the elderly.

2. Methods

2.1. Setting and study design

This study was a retrospective cohort study at a single tertiary hospital in Japan that was a core hospital in the area. We enrolled patients who were 75 years or older, who were hospitalized urgently, and who underwent mechanical ventilation between January 1, 2014 and December 31, 2017. The indication for mechanical ventilation was provided by a trained emergency physician. The definition of performing mechanical ventilation was defined as tracheal intubation for at least 6 hours within 24 hours from the hospital visit and the patient receiving intensive care. Patients were excluded from the analysis for the following reasons:

1. they were intubated for less than 6 hours;
2. they were trauma patients;
3. they were cardiopulmonary arrest patients at a hospital visit;
4. they had an airway emergency (tracheostomy or cricothyroid incision within 12 hours of hospital visit); or
5. they received mechanical ventilation management after 24 hours of hospitalization.

2.2. Study variables

The following data were extracted from medical records and considered to be confounding factors based on previous research:[5,7,8,15–18] age, gender, BMI, smoking history (never-smoker, ex-smoker, current-smoker), ADL (independent: almost independent in daily life and goes out by themself; house-bound: indoor life is largely self-supported but does not go out without assistance; chair-bound: living indoors requires some kind of assistance, mainly lives on a bed during the day, but maintains a sitting position; bed-bound: spends the day in bed and requires assistance with defecation, eating, and changing clothes), comorbidities[8,16] (diabetes mellitus: patients who use insulin or oral hypoglycemic drugs, who have a history of diabetes in medical records; heart disease: patients with a history of angina or myocardial infarction or heart failure in medical records; obstructive pulmonary disease: patients with a history of obstructive pulmonary disease in medical records or with inhaled drugs for obstructive pulmonary disease, leukotriene antagonist, aminophylline; cancer: patients with untreated or currently treated cancer; kidney failure: glomerular filtration rate [GFR] less than 15 ml/minutes/1.73 m^2), severity of concurrent illness when attending the emergency room (a modified APACHE II score[7,17]), and initial diagnosis at the hospital visit (e.g., disease of the respiratory system, disease of the nervous system, disease of the circulatory system, disease of the digestive system, disease of the genitourinary system, and sepsis). The diagnosis at the hospital visit was made by the emergency physician and classified based on the International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD-10) and the Third International Consensus Definitions for Sepsis and Septic Shock.[19]

2.3. Clinical outcome

The primary outcome was extubation difficulty, which was defined as the need for mechanical ventilation more than 14 days after intubation, reintubation within 72 hours after extubation, tracheotomy, and death within 14 days after intubation. Although prolonged mechanical ventilation is often defined as greater than 21 days of mechanical ventilation for at least 6 hours per day,[20,21] in this study, 14 days, which is the standard for tracheostomy in Japan, was used as the cut-off point. The judgment for extubation was made by a well-trained intensive care physician. Furthermore, in the extubation difficulty group, a comparison was made between the non-death within 14 days group and the death group.

2.4. Study size

Because this was an observational study that encompassed an exploratory study, strict sample size settings were not used. The sample size was determined from the number of cases in the study sites within the study period.

2.5. Statistical analysis

Statistical analysis was conducted using STATA version 12.1 (Stata-Corp, College Station, TX, USA). Continuous variables are shown as the median value with 25th and 75th percentiles. Categorial data are shown as the percentage with patient numbers. We used the Mann–Whitney *U*-test to compare the non-normally distributed continuous variables and Pearsons Chi-Squared test or Fishers exact test to compare the proportions of categorial variables between the extractable group and the extubation difficulty group. To determine risk factors for extubation difficulty, a multivariate analysis was performed using multiple logistic regression. Based on clinical judgments and previous research findings, variables that were considered to be relevant to the outcome, and variables with a P value $<.10$ in the univariate analysis were included in the multivariable models. All statistical analyses were two-sided, and the threshold for significance was a P value $<.05$. For missing data, we performed a complete case analysis that excluded the data of those who were missing at least one of the specified independent and dependent variables.

2.6. Ethical considerations

Because the study did not acquire new samples and information, the requirement for written or verbal informed consent was waived. Information about the study was published on the website of the research institute, and the opportunity for refusal was guaranteed. Study approval was obtained from the institutional review board at the National Hospital Organization Nagasaki Medical Center.

2.7. Patient and public involvement

Neither patients nor the public were involved in the design, conduct, reporting, or dissemination plans of our research.

3. Results

Figure 1 shows the study flow. During the study period, 427 patients who were over 75 years of age who were hospitalized urgently and underwent mechanical ventilation were enrolled, and 228 patients met the study inclusion criteria. Patients were excluded from the analysis if intubation was less than 6 hours (n = 199), or if the patient was a trauma patient (n = 95), a cardiopulmonary arrest patient at a hospital visit (n = 15), had an

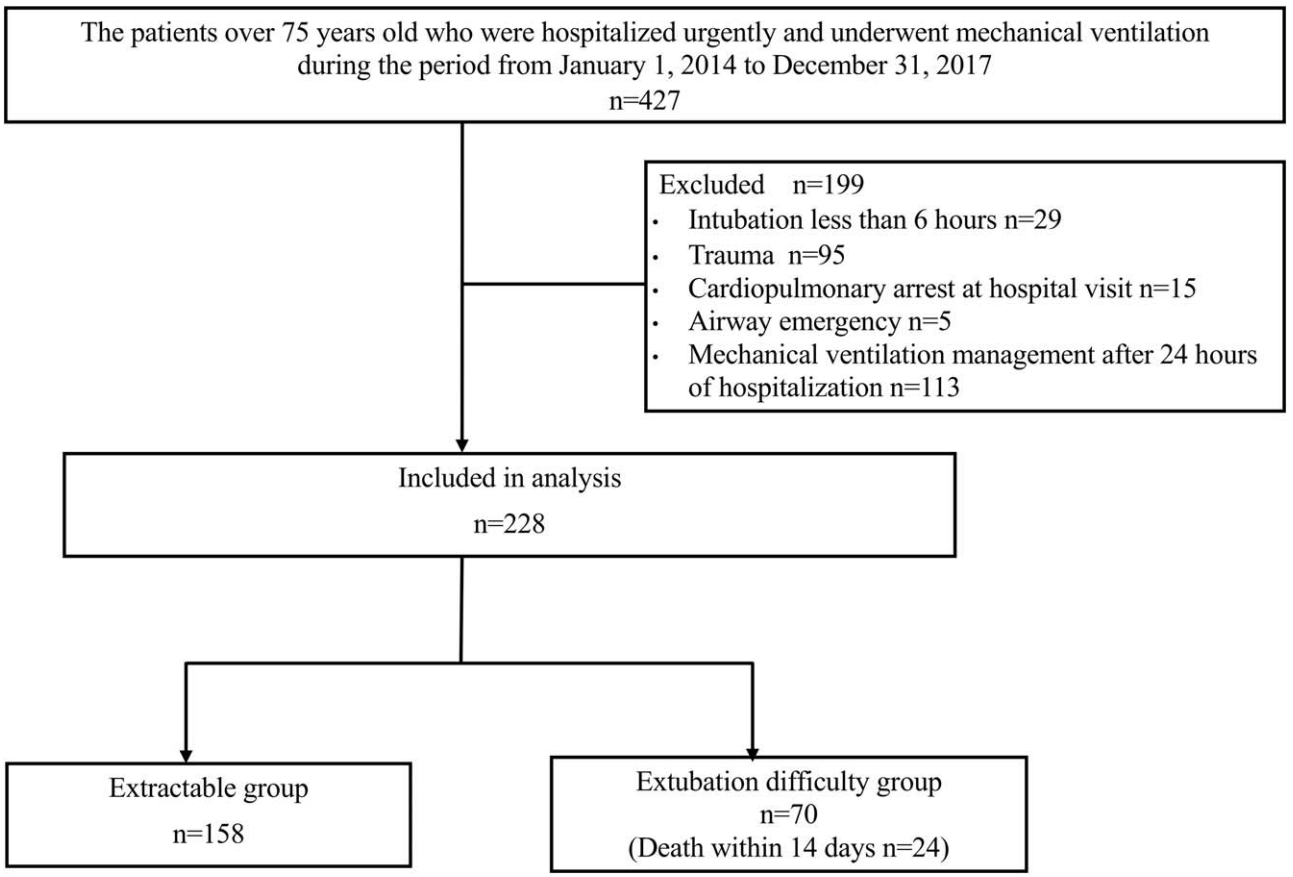

Figure 1. Flow of participants.

airway emergency (n = 5), or required mechanical ventilation management after 24 hours of hospitalization (n = 113). Thus, 228 patients were included in the analysis. Among the 228 patients, 158 were in the extractable group and 70 were in the extubation difficulty group. Table 1 shows the demographic and clinical characteristics of 228 patients, and Tables 2 and 3 show the factors that were associated with the risk of extubation difficulty using univariate and multivariate logistic regression analyses. In the univariate analysis, there were no statistically significant differences between any of the variables except for circulatory system diagnoses at the hospital visit (odds ratio, OR = 0.31; 95% confidence interval, [CI] = 0.10–0.92; $P = .04$). In multivariate analysis using multivariate logistic regression, there were no statistically significant differences in age (OR = 0.95; 95% CI = 0.66–1.38; $P = .80$), gender (OR = 0.56; 95% CI = 0.27–1.17; $P = .13$), BMI (OR = 1.05; 95% CI = 0.98–1.14; $P = .16$), smoking history (OR = 0.64; 95% CI = 0.29–1.41; $P = .27$), ADL (OR = 0.95; 95% CI = 0.49–1.83; $P = .87$), and modified APACHE II score (OR = 1.02; 95% CI = 0.95–1.09; $P = .61$). However, there were statistically significant differences in the diagnosis of diabetic co-morbidities (OR = 2.30; 95% CI = 1.01–5.12; $P = .04$) and diagnoses of the circulatory system at the hospital visit (OR = 0.31; 95% CI = 0.10–0.97; $P = .04$). Table 4 presents a comparison between the non-death group (n = 45) and the death group (n = 25) in the extubation difficulty group (n = 70). In the death group, there were a statistically significant number of males. Table 5 shows the details of the cardiovascular disease at the time of the hospital visit that caused the intubation.

4. Discussion

4.1. Brief summary and comparison with previous studies

The main finding of this study was that diabetes mellitus diagnosis and cardiovascular disease diagnosis at the time of hospital visit was a statistically significant factor related to difficulty in extubation for the elderly. However, the results of this study showed no statistically significant difference between age, gender, BMI, smoking history, ADL, hospital severity, and extubation difficulty. Although univariate analysis revealed that a cardiovascular disease diagnosis at the time of hospital visit underestimated the association between diabetes mellitus and extubation difficulties and was not significantly different, we believe that adjustment for multivariate analysis would have resulted in a more accurate association.

The I-TRACH (Intubation in the ICU, Tachycardia [heart rate >110], Renal dysfunction [blood urea nitrogen >25], Acidemia [pH < 7.25], Creatinine [>2.0 or >50% increase from baseline values], and decreased HCO_3 [<20]) score, a clinical predictor of long-term respiratory management, has been reported but it is not limited to the elderly.[22] There are few previous studies that have clarified the predictors of extubation difficulty for the elderly only based on factors that are found in the emergency room.[23] There are reports suggesting an association between diabetes mellitus and prolonged mechanical ventilation.[24,25]

Non-invasive positive pressure ventilation was excluded in this study. Intubation can be avoided in most cases of acute exacerbation of heart failure using non-invasive positive pressure

Table 1

Demographic and clinical characteristics of the 228 patients enrolled into this study.

	All patients N = 228	Extractable group N = 158	Extubation difficulty group N = 70	*P* value
Age (years)	82 [78, 85]	82 [78, 85]	82 [78, 87]	.75
Male (N, %)	112 (49%)	74 (47%)	38 (54%)	.30
BMI (kg/m^2)	21 [18, 23]	20 [18, 22]	21 [18, 23]	.19
Smoking history (N, %)				.87
Never smoker	141 (62%)	96 (61%)	45 (64%)	
Ex-smoker	73 (32%)	53 (34%)	20 (29%)	
Current smoker	10 (4.4%)	6 (3.8%)	4 (5.7%)	
Missing data*	4 (1.8%)	3 (1.9%)	1 (1.4%)	
ADL (N, %)				.87
Independent	137 (60%)	93 (59%)	44 (63%)	
House-bound	59 (26%)	43 (27%)	16 (23%)	
Chair-bound	19 (8.3%)	12 (7.6%)	7 (10%)	
Bed-bound	4 (1.8%)	3 (1.9%)	1 (1.4%)	
Missing data*	9 (3.9%)	7 (4.4%)	2 (2.9%)	
modified APACHE II score	11 [9, 15.5]	11 [9, 15]	12.5 [9, 16]	.26
Comorbidities (N, %)				
Diabetes mellitus	34 (15%)	19 (12%)	15 (21%)	.066
Heart disease	58 (25%)	39 (25%)	19 (27%)	.69
Obstructive pulmonary disease	23 (10%)	15 (9.5%)	8 (11%)	.65
Cancer	6 (2.7%)	6 (3.8%)	0 (0%)	.98
Kidney failure	4 (1.8%)	2 (1.3%)	2 (2.9%)	.40
Initial diagnosis (N, %)				
Respiratory system	40 (18%)	27 (17%)	13 (19%)	.79
Nervous system	88 (39%)	63 (40%)	25 (36%)	.55
Circulatory system	30 (13%)	26 (17%)	4 (5.7%)	.027
Digestive system	64 (28%)	43 (27%)	21 (30%)	.67
Genitourinary system	1 (0.4%)	0 (0%)	1 (1.4%)	.13
Sepsis	47 (21%)	28 (18%)	19 (27%)	.10
Miscellaneous	13 (5.7%)	4 (2.5%)	9 (13%)	.002

* Missing data indicates that the patient's data were missing in the medical records.

Continuous variables were expressed as the median [25%, 75% percentile]. Categorized variables are expressed as the number (percentile).

ADL = activities of daily living, BMI = body mass index.

Table 2

Factors associated with the risk for extubation difficulty using univariate logistic regression analysis.

	Univariate analysis	
Variables	**Crude OR (95%CI)**	***P* value**
Age, per 5-year increment	0.95 (0.68–1.34)	.78
Female (versus male)	0.74 (0.42–1.30)	.30
BMI	1.06 (0.99–1.13)	.12
Smoker (versus non-smoker)	0.87 (0.48–1.57)	.64
ADL independent (versus dependent)	0.87 (0.48–1.59)	.66
Modified APACHE II score	1.02 (0.97–1.09)	.39
Diabetes mellitus	2.00 (0.95–4.20)	.07
Heart disease	1.13 (0.60–2.15)	.60
Obstructive pulmonary disease	1.23 (0.50–3.10)	.66
Cancer	-	-
Kidney failure	2.29 (0.32–16.6)	.41
Respiratory system diagnosis	1.11 (0.53–2.30)	.79
Nervous system diagnosis	0.84 (0.47–1.50)	.55
Circulatory system diagnosis	0.31 (0.10–0.92)	.04
Digestive system diagnosis	1.15 (0.62–2.13)	0.67
Genitourinary system diagnosis	-	-
Sepsis diagnosis	1.73 (0.89–3.37)	.11

ADL = activities of daily living, BMI = body mass index, CI = confidence interval, OR = odds ratio.

ventilation. Acute aortic dissection, ruptured aortic aneurysm, acute myocardial infarction, and congestive heart failure were common intubation-causing cardiovascular diseases in this study, as shown in Table 5. For respiratory insufficiency caused by these circulatory diseases, extubation difficulty was less likely to occur. Even elderly patients may be considered for initiation of intensive care, including intubation and mechanical ventilation. Additionally, age was not statistically associated with long-term ventilator management in this study. Age has been reported to be a prognostic predictor in respiratory failure resulting from acute respiratory distress syndrome (ARDS),[26] while several other previous studies suggested that age is not a major factor associated with long-term ventilatory management.[6,7,14] Intensive care should not be withheld solely based on chronological age.

4.2. Possible explanations and implications

Appropriate shared decision-making is critical in geriatric care. However, there is a lack of decision-making support regarding the initiation of intensive care for the elderly.[27,28] Prolonged mechanical ventilation in the elderly is an important outcome that affects the subsequent costs, the patients quality of life, and the caregivers burden of care.[8–11,29] It has been reported that individual physicians provide information on their own experi-

Table 3

Factors associated with the risk for extubation difficulty using a multivariate logistic regression analysis.

	Multivariate analysis	
Variables	**Adjusted OR (95%CI)**	***P* value**
Age, per 5-year increment	0.95 (0.66–1.38)	.80
Female (versus male)	0.56 (0.27–1.17)	.13
BMI	1.05 (0.98–1.14)	.16
Smoker (versus non-smoker)	0.64 (0.29–1.41)	.27
ADL independent (versus dependent)	0.95 (0.49–1.83)	.87
Modified APACHE II score	1.02 (0.95–1.09)	.61
Diabetes mellitus	2.30 (1.01–5.12)	.04
Circulatory system diagnosis	0.31 (0.10–0.97)	.04

ADL = activities of daily living, BMI = body mass index, CI = confidence interval, OR = odds ratio.

ence regarding the prediction, but the prediction accuracy is low.[30,31] It is important to be able to predict subsequent extubation difficulty before the decision to intubate is made in the emergency room. The results of this study may be useful in supporting decision-making for patients, their families, and proxy decision-makers. This may be useful for the development of a future clinical prediction rule.

4.3. Limitations

This study had some limitations, including the small sample size during the planned study period, which might have decreased the studys power. Second, because the study was conducted at a single institution, the regional and institutional characteristics of the criteria for intubation and extubation were not adjusted. Finally, patients with extubation difficulty that was strongly predicted by the clinicians judgment or who did not intend to start intubation or be placed onto a ventilator were excluded. Although there is no standardized protocol for intubation and extubation at the research institution, this does not significantly deviate from the guidelines[32] and it is not considered to be a major limitation.

5. Conclusion

We examined which factors at the time of the hospital visit were associated with subsequent extubation difficulty for elderly people aged 75 years or older who were ventilated as a result of any intrinsic disease. There was no statistically significant difference in age, ADL, or severity, although diabetes mellitus and cardiovascular disease diagnoses at the visit were statistically significantly associated with subsequent extubation difficulty.

Table 4

The non-death within 14 days group is compared to the death group in the extubation difficulty group.

	Extubation difficulty group N = 70	Non-death group N = 45	Death group N = 25	*P* value
Age (years)	82 [78, 87]	82 [78, 85]	83 [78, 89]	.27
Male (N, %)	38 (54%)	16 (36%)	16 (64%)	.022
BMI (kg/m^2)	21 [18, 23]	21 [17, 23]	21 [20, 23]	.34
Smoking history (N, %)				.21
Never smoker	45 (64%)	27 (60%)	18 (75%)	
Ex-smoker	20 (29%)	16 (36%)	4 (17%)	
Current smoker	4 (5.7%)	2 (4%)	2 (8%)	
Missing data*	1 (1.4%)	0 (0%)	1 (4%)	
ADL (N, %)				.90
Independent	44 (63%)	29 (64%)	15 (65%)	
House-bound	16 (23%)	11 (24%)	5 (22%)	
Chair-bound	7 (10%)	4 (9%)	3 (13%)	
Bed-bound	1 (1.4%)	1 (2%)	0 (0%)	
Missing data*	2 (2.9%)	0 (0%)	2 (8%)	
modified APACHE II score	12.5 [9, 16]	12 [9, 18]	13 [10, 16]	.59
Comorbidities (N, %)				
Diabetes mellitus	15 (21%)	11 (24%)	4 (16%)	.41
Heart disease	19 (27%)	13 (29%)	6 (24%)	.66
Obstructive pulmonary disease	8 (11%)	5 (11%)	3 (12%)	.91
Cancer	0 (0%)	0 (0%)	0 (0%)	-
Kidney failure	2 (2.9%)	0 (0%)	2 (8%)	.054
Initial diagnosis (N, %)				
Respiratory system	13 (19%)	7 (16%)	6 (24%)	.38
Nervous system	25 (36%)	18 (40%)	7 (28%)	.32
Circulatory system	4 (5.7%)	2 (4%)	2 (8%)	.54
Digestive system	21 (30%)	14 (31%)	7 (28%)	.79
Genitourinary system	1 (1.4%)	1 (2%)	0 (0%)	.45
Sepsis	19 (27%)	9 (20%)	10 (40%)	.071
Miscellaneous	9 (13%)	6 (13%)	3 (12%)	.87

* Missing data indicates that the patient's data were missing in the medical records.

Continuous variables were expressed as the median [25%, 75% percentile]. Categorized variables are expressed as the number (percentile).

ADL = activities of daily living, BMI = body mass index.

Table 5

Details of cardiovascular disease as a reason for intubation.

	All patients N = 30	Extractable group N = 26	Extubation difficulty group N = 4
Acute aortic dissection	13 (43%)	13	0
Ruptured aortic aneurysm	5 (17%)	4	1
Congestive heart failure	5 (17%)	4	1
Acute myocardial infarction	4 (13%)	3	1
Pulmonary embolism	1 (3%)	1	0
Acute myocarditis	1 (3%)	1	0
Sick sinus syndrome	1 (3%)	0	1

Categorized variables are expressed as the number (percentile).

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Author contributions

HM was responsible for organization and coordination of the trial. KY, TI, YS, YT, TM, TO, and YI provided substantial contributions to the conception or design of the work or the acquisition, analysis or interpretation of data, and revised the manuscript critically for important intellectual content. All authors contributed to writing the final manuscript.

Conceptualization: Hideki Mori, Kazumi Yamasaki, Takehiro Itoh, Yusuke Saishoji, Yuichi Torisu, Takahiro Mori, Yasumori Izumi.
Data curation: Hideki Mori, Kazumi Yamasaki, Takehiro Itoh, Yasumori Izumi.
Formal analysis: Hideki Mori, Kazumi Yamasaki, Takehiro Itoh, Yasumori Izumi.
Investigation: Hideki Mori.
Methodology: Hideki Mori.
Project administration: Hideki Mori, Kazumi Yamasaki, Yusuke Saishoji.
Software: Hideki Mori.
Supervision: Kazumi Yamasaki, Yasumori Izumi.
Validation: Hideki Mori.
Visualization: Hideki Mori.
Writing – original draft: Hideki Mori.
Writing – review & editing: Hideki Mori, Kazumi Yamasaki, Takehiro Itoh, Yusuke Saishoji, Yuichi Torisu, Takahiro Mori, Yasumori Izumi.

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