

ORIGINAL**Prognosis of frail older patients treated with intubation and artificial ventilation for respiratory failure**

Kazuhiisa Nakashima, Ken Yoshihara, Kento Kono, Mika Horie, Seiko Tanaka, Keita Kawakado, Misato Kobayashi, Yohei Shiratsuki, Takae Okuno, Mika Nakao, Yoshihiro Amano, Takamasa Hotta, Megumi Hamaguchi, Shunichi Hamaguchi, Yukari Tsubata, Taishi Nagao, Noriaki Kurimoto, and Takeshi Isobe

Department of Internal Medicine, Division of Medical Oncology & Respiratory Medicine, Shimane University Faculty of Medicine, Shimane, Japan

Abstract : *Background :* Older patients with severe respiratory failure have higher mortality rates and are more likely to experience impairments in activities of daily living (ADL). *Methods :* We retrospectively reviewed patients (≥ 75 years) who received intubation and artificial ventilation for respiratory failure at Shimane University Hospital between November 2014 and December 2020. We compared the outcomes of frail patients with those of self-sufficient patients. *Results :* Thirty-two patients were included. ADL ability before respiratory failure was rated self-sufficient in 18 patients (self-sufficient group) and not self-sufficient in 14 patients (frail group). None of the patients in either group underwent advanced care planning prior to the onset of respiratory failure. In the self-sufficient and frail groups, the in-hospital mortality rates were 33% and 50%, and the incidence of bedridden patients at discharge was 6% and 43%, respectively. Most patients in the frail group (93%) died or were bedridden. The median hospitalization cost was JPY 2,984,000 for the self-sufficient group and JPY 3,008,000 for the frail group. *Conclusion :* The overall prognosis of frail older patients who underwent intubation and artificial ventilation was poor. When providing intensive care to such patients, it is important to carefully consider their suitability for the treatment. *J. Med. Invest. 70 : 494-498, August, 2023*

Keywords : *artificial ventilation, frail, intubation, older patients, respiratory failure*

INTRODUCTION

In Japan, societal aging has been progressing rapidly (1), and the incidence of death due to respiratory diseases such as pneumonia is increasing in older people (2). Although intubation and artificial ventilation are indicated for patients with severe respiratory failure, older patients have a high mortality rate and are more likely to have impaired physical function and activities of daily living (ADL) (3-6). The intensive care required for treatment is associated with high medical costs (3, 4); however, no studies to date have investigated this issue in Japan. Moreover, advanced-care planning (ACP) plays a significant role in protecting individual dignity (7), but it is not yet prevalent in Japan (8, 9). Few previous reports have discussed whether the intensive care provided was compliant with the wishes of older Japanese patients with respiratory failure and their families.

Intensive treatment of respiratory failure can be a heavy burden on the patient owing to its invasiveness and high cost. In older patients, correct judgement about the necessity of such treatment is important in order to avoid excessive treatment, which may result in poorer quality of life and functional prognosis in frail patients. Therefore, this retrospective study aimed to compare the prognosis, ADL after treatment, and medical cost incurred, of frail older patients who received intubation and artificial ventilation for severe respiratory failure with those of self-sufficient patients.

PATIENTS AND METHODS*Patients*

We retrospectively reviewed older patients who received intubation and artificial ventilation as treatment for respiratory failure at Shimane University Hospital between November 2014 and December 2020. In Japan, an institution with 600 beds is considered a general hospital. The eligible patients included cases in which the respiratory status of inpatients worsened and patients presented to the emergency room with severe respiratory failure. When non-invasive oxygen therapy failed to maintain adequate oxygenation, intubation and artificial ventilation were considered. Specifically, "older" patients were defined as those aged ≥ 75 years based on the Japan Gerontological Society and the Japan Geriatrics Society recommendations (10). We excluded cases of cardiopulmonary arrest of uncertain etiology.

Assessment and statistical analysis

We retrospectively collected patients' clinical information from their medical records. We assessed the patient characteristics, treatments, outcomes, survival time, and costs of intubation and artificial ventilation treatment in older patients with severe respiratory failure. Medical costs were the total hospitalization costs at our institution, calculated by the medical affairs division staff. Patient characteristics included age, sex, baseline ADL ability, Charlson Comorbidity Index, presence or absence of ACP before respiratory failure onset, and the cause of respiratory failure. We decided that ACP was not conducted if there was no record about the willingness of the patient for invasive treatment or resuscitative efforts in worsening condition, or discussion of end of life. Treatments included the period of artificial ventilation use, intensive care unit (ICU) stay duration, hospital stay duration, and the presence or absence of physical rehabilitation.

Received for publication March 16, 2023 ; accepted August 28, 2023.

Address correspondence and reprint requests to Yukari Tsubata, MD, PhD, Department of Internal Medicine, Division of Medical Oncology & Respiratory Medicine, Shimane University Faculty of Medicine, 89-1 Enya-cho, Izumo, Shimane 693-8501, Japan and Fax : +81-853-20-2581. E-mail : ytsubata@med.shimane-u.ac.jp

The ICU discharge criteria involved confirming respiratory stability after extubation, or in cases where extubation was difficult, ensuring stable management of artificial ventilation after tracheostomy. The discharge criteria included the completion of acute-phase treatment. Outcomes included discharge destination and ADL ability at discharge.

Baseline ADL were not sufficiently assessed with well-established tools, such as the Barthel Index or Lawton Instrumental ADLs (11, 12), because most patients presented to the emergency room with rapid-onset disease. Therefore, in this study, we broadly classified ADL as “self-sufficient,” “requiring some assistance or care,” or “bedridden.” “Self-sufficient” is more or less equal to Clinical Frailty Scale (CFS : a tool to classify the condition of older people to 9 levels) 1-3, “requiring some assistance or care” is more or less equal to CFS 4-6, and “bedridden” is more or less equal to CFS 7-9 (13). We defined patients of “requiring some assistance or care” and “bedridden” as frail group. We compared the outcomes of baseline frailty patients with those of self-sufficient patients.

Fisher’s exact test was used to compare the mortality and bedridden rates. Overall survival (OS) after intubation was evaluated using the Kaplan-Meier method. Analyses were performed using JMP software (version 10.0 ; SAS Institute, Cary, NC, USA).

Ethics

The retrospective study protocol was approved by our institutional review board (approval number : 5413 ; approval date : April 14, 2021), who waived the requirement of informed consent.

RESULTS

Patient characteristics

Thirty-two older patients (age range : 77–95 years ; 23 men and 9 women) were enrolled in this study. Patient characteristics

are shown in Table 1. The self-sufficient group included 18 patients, and the frail group included 14 patients (10 patients required some assistance or care, and 4 patients were bedridden). Most patients (72%) underwent intubation at the visit to the emergency room. Bacterial pneumonitis was the most common cause of respiratory failure (N = 11). Aspiration pneumonitis was also more common in the frail group. None of the patients underwent ACP before the onset of respiratory failure.

Treatments and outcomes

Treatments and outcomes are shown in Table 2. The median period of artificial ventilation use, duration of ICU stay, and hospital stay were longer in the frail group than in the self-sufficient group. The in-hospital mortality rates were 41% (n = 13) in all patients, 33% (n = 6) in the self-sufficient group, and 50% (n = 7) in the frail group (p = 0.47). Although most patients underwent physical rehabilitation at the hospital, none of the patients in either group was completely self-sufficient at discharge (Figure 1). In the self-sufficient group, only 39% of patients died or were bedridden ; however, in the frail group, most of the patients (93%) died or were bedridden (p = 0.0028).

The outcome subgroup analysis by age (75-84 years old vs >85 years old) is shown in Table 3. Among 75-84 years old patients, ten (56%) died and four (22%) were bedridden. In contrast, among patients aged ≥ 85 years old, three (21%) died, and three (21%) were bedridden.

The median overall survival was 1299 days in the self-sufficient group and 96 days in the frail group (Figure 2). We could not conduct a follow-up of the eight patients who were discharged.

Medical cost

The median hospitalization costs were JPY 2,984,000 (22,800 USD) in the self-sufficient group and JPY 3,008,000 in frail group (23,000 USD).

Table 1. Patient characteristics

	All N = 32	Self-sufficient group N = 18	Frail group N = 14
Median age (range)	84 (77-95)	84 (79-95)	84 (77-92)
Male	23 (72%)	14 (78%)	9 (64%)
Female	9 (28%)	4 (22%)	5 (36%)
ADL before respiratory failure :			
Self-sufficient	18 (56%)	18 (100%)	0
Requiring some assistance or care	10 (31%)	0 (0%)	10 (71%)
Bedridden	4 (13%)	0 (0%)	4 (29%)
Cause of respiratory failure			
Bacterial pneumonitis	11 (34%)	5 (28%)	6 (43%)
Aspiration pneumonitis	6 (19%)	1 (6%)	5 (36%)
Hemoptysis	4 (13%)	4 (22%)	0 (0%)
COPD	3 (9%)	1 (6%)	2 (14%)
Interstitial pneumonia	3 (9%)	3 (17%)	0 (0%)
Other	5 (16%)	4 (22%)	1 (7%)
Median CCI	6	6	6

ADL, activities of daily living ; CCI, Charlson Comorbidity Index ; COPD, chronic obstructive pulmonary disease ; CFS, Clinical Frailty Scale.

Table 2. Patient treatments and outcomes

	All N = 32	Self-sufficient group N = 18	Frail group N = 14	p
Median period of artificial ventilation use	9 days	7.5 days	13.5 days	
Median ICU stay duration	11 days	10.5 days	16.5 days	
Median hospital time	36 days	33.5 days	50 days	
Patients who received rehabilitation	26 (81%)	17 (94%)	9 (64%)	
Outcome :				
Death	13 (41%)	6 (33%)	7 (50%)	0.47*
Transferred to another hospital	13 (41%)	7 (39%)	6 (43%)	
Discharged to home	5 (16%)	4 (22%)	1 (7%)	
Transferred to a nursing care facility	1 (3%)	1 (6%)	0 (0%)	
ADL ability at discharge :				
Self-sufficient	0 (0%)	0 (0%)	0 (0%)	
Requiring some assistance or care	12 (38%)	11 (61%)	1 (7%)	
Bedridden	7 (22%)	1 (6%)	6 (43%)	0.027**

ICU, intensive care unit ; ADL, activities of daily living ; CFS, Clinical Frailty Scale.

*The p-value pertains to the mortality rate. **The p-value pertains to the bedridden rate.

Table 3. Subgroup analysis

	All N = 32	Self-Sufficient group N = 18	Frail group N = 14	75-84 years n = 18	85+ years n = 14
Mortality	41%	33%	50%	56%	21%
Bedridden at discharge	22%	6%	43%	22%	21%
Total (death or bedridden)	63%	39%	93%	78%	43%
		p = 0.0028*		p = 0.068*	

*The p-value pertains to the total rate (death or bedridden).

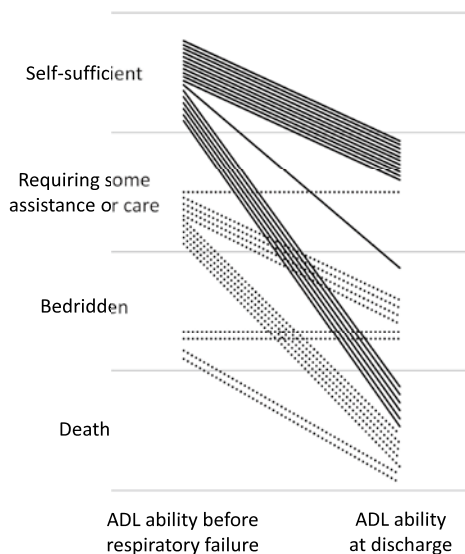


Figure 1. Changes in activities of daily living (ADL) among discharged survivors. The self-sufficient group is shown by a solid line, and the frail group is shown by a dotted line. “Self-sufficient” is approximately equal to Clinical Frailty Scale (CFS) of 1-3, “requiring some assistance or care” is approximately equal to CFS of 4-6, and “bedridden” is approximately equal to CFS of 7-9.

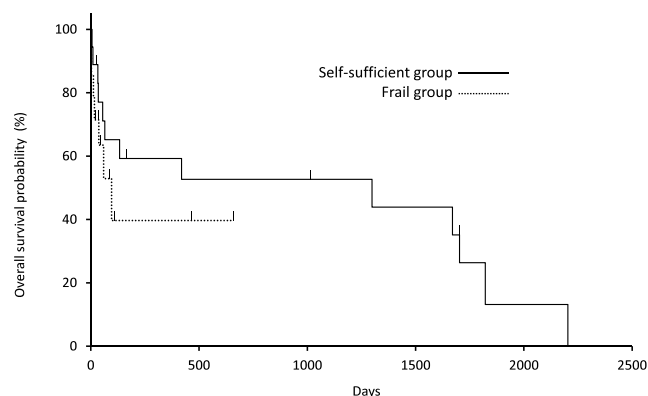


Figure 2. Kaplan-Meier curve of the overall survival (OS) of patients. The median OS was 1299 days in self-sufficient group, and 96 days in frail group (p = 0.95).

DISCUSSION

This retrospective study evaluated the prognosis following the use of intubation and artificial ventilation in the treatment of frail elderly patients with severe respiratory failure. In a prospective cohort study, Dardaine *et al.* reported that in patients aged ≥ 70 years who were admitted to the ICU and treated with mechanical ventilation, the mortality rates in the ICU and 6 months after discharge were 31% and 52%, respectively (5). The mortality rate of all patients at discharge in our study was high (41%), similar to that in previous reports (3-6). In the self-sufficient and frail groups, the in-hospital mortality rates were 33% and 50%, and the percentage of patients who were bedridden at discharge was 6% and 43%, respectively. Most of the patients in the frail group (93%) died or were bedridden. Low baseline ADL ability was a poorer prognostic factor than age ≥ 85 years (The more favorable prognosis among those aged ≥ 85 years might have been influenced by the relatively low proportion of bedridden patients at baseline [75-84 years : 17%, and ≥ 85 years : 7%]). Therefore, intubation and artificial ventilation should be avoided in frail older patients. In contrast, the life prognosis in the self-sufficient group was favorable (median overall survival, 1299 days). Intubation and artificial ventilation should be considered for self-sufficient patients with severe respiratory failure.

The median hospitalization costs were similar in both groups : JPY 2,984,000 in the self-sufficient group and JPY 3,008,000 in the frail group. There was no cost disadvantage for the frail group compared to the self-sufficient group. However, very high medical costs were incurred on intensive treatment. Although balancing cost with human life is difficult, this treatment for frail patients may not be clinically or economically justifiable.

ACP is important for protecting the dignity of individuals (7). None of the patients in this retrospective study underwent ACP before respiratory failure. Similar to previous reports (8, 9), our results reinforce the fact that ACP is not yet widespread in Japan. This may be because of the Japanese cultural norms that value sociality (their loved ones' preferences) over the wishes of an individual (14). In addition, Japanese tend to believe that the unawareness of death is important for a good death (15). Although we obtained informed consent from the patient or family members for performing intubation in this study, there may not always be enough time and emotional leeway to make calm judgments in emergency situations. Excessive treatment might be avoided by ACP. Therefore, medical doctors and staff in Japan should encourage the use of ACP.

This study had several limitations. First, it was a retrospective study performed at a single center with a small sample size. Although we initially defined the "frail group" on the basis of Clinical Frailty Scale of 4-9, it may have been more appropriate to define it on the basis of Clinical Frailty Scale of 7-9. Unfortunately, our analysis using the Clinical Frailty Scale 7-9 range was limited due to the inclusion of only four cases in this category. Second, the older patients comprised a heterogeneous population with age-related changes and comorbidities. The causes of respiratory failure varied. Third, ADL was assessed using a rough scale because most patients presented to the emergency room with rapid-onset disease. Fourth, follow-up after discharge was not performed for some patients. Dardaine *et al.* reported that most older patients (aged ≥ 70 years) requiring ventilatory support in the ICU had a similar or improved functional status compared to the pre-admission status (5). In some patients, ADL may be improved by long-term rehabilitation. Although this study included these limitations, the results are useful for deciding whether intubation should be performed in older patients with respiratory failure because performing a prospective study

on this topic is comparatively difficult. Further retrospective studies with larger sample sizes and comparisons are warranted. Moreover, a tool to distinguish patients with a good prognosis from those with a poor prognosis is needed.

CONCLUSION

The life and functional prognoses of frail older patients who underwent intubation and artificial ventilation were poor. Hospitalization costs were high. When providing intensive care to such patients, it is important to carefully consider their suitability for the treatment.

FUNDING

This study did not receive any specific grants from funding agencies in the public, commercial, or non-profit sectors.

CONFLICTS OF INTEREST

There are no conflicts of interest to declare.

ACKNOWLEDGMENTS

We would like to thank Mr. Takaaki Sonoyama of the Medical Affairs Division staff at Shimane University Hospital for his instructions regarding medical costs and Editage (www.editage.com) for English language editing.

REFERENCES

1. Statistics Bureau of Japan : Result of the population estimates, <https://www.stat.go.jp/index.html>. [accessed 12 March 2023].
2. Ministry of Health, Labour and Welfare : Vital statistics, <https://www.mhlw.go.jp/english/index.html>. [accessed 12 March 2023].
3. Hamel MB, Phillips RS, Davis RB, Teno J, Connors AF, Desbiens N, Lynn J, Dawson NV, Fulkerson W, Tsevat J : Outcomes and cost-effectiveness of ventilator support and aggressive care for patients with acute respiratory failure due to pneumonia or acute respiratory distress syndrome. *A Am J Med* 109 : 614-620, 2000
4. Hamel MB, Phillips RS, Davis RB, Teno J, Desbiens N, Lynn J, Tsevat J : Are aggressive treatment strategies less cost-effective for older patients? The case of ventilator support and aggressive care for patients with acute respiratory failure. *J Am Geriatr Soc* 49 : 382-390, 2001
5. Dardaine V, Dequin PF, Ripault H, Constans T, Giniès G : Outcome of older patients requiring ventilatory support in intensive care : impact of nutritional status. *J Am Geriatr Soc* 49 : 564-570, 2001
6. El Solh AA, Bhat A, Gunen H, Berbary E : Extubation failure in the elderly. *Respir Med* 98 : 661-668, 2004
7. Detering KM, Hancock AD, Reade MC, Silvester W : The impact of advance care planning on end of life care in elderly patients : randomised controlled trial. *BMJ* 340 : c1345, 2010
8. Cheng SY, Lin CP, Chan HY, Martina D, Mori M, Kim SH, Ng R : Advance care planning in Asian culture. *Jpn J Clin Oncol* 50 : 976-989, 2020

9. Takazono T, Imamura Y, Kawakami K, Yamasaki N, Shimizu H, Usuki K, Kiyohara M, Hirayama T, Tashiro M, Hosogaya N, Saijo T, Yamamoto K, Miyazaki T, Yanagihara K, Izumikawa K, Mukae H : Discrepancies in preferences regarding the care of terminal-phase pneumonia in elderly patients among patients, families, and doctors : A multi-center questionnaire survey in nagasaki, Japan. *Respir Investig* 58 : 488-494, 2020
10. The Japan geriatrics Society : The definition of "old", https://www.jpn-geriat-soc.or.jp/proposal/pdf/definition_01.pdf. [accessed 12 March 2023].
11. Mahoney FI, Barthel DW : Functional evaluation : the Barthel index. *Md State Med J* 14 : 61-65, 1965
12. Lawton MP, Brody EM : Assessment of older people : self-maintaining and instrumental activities of daily living. *Gerontologist* 9 : 179-186, 1969
13. Clinical Frailty Scale 2005-2020 Rockwood, Version 2.0 (JA), <https://www.dal.ca/sites/gmr.html> [accessed 12 March 2023]
14. Bito S, Wenger NS, Ohki M, Fukuhara S : Japanese attitude toward advance care planning for end-of-life decisions. *Gen Med* : 3-10, 2001
15. Miyashita M, Sanjo M, Morita T, Hirai K, Uchitomi Y : Good death in cancer care : a nationwide quantitative study. *Ann Oncol* 18 : 1090-1097, 2007