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Original Article

Character and Outcome of Geriatric Patients with Do-Not-Resuscitate Orders after Receiving Non-invasive Ventilation in the Emergency Room

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SUMMARY

Objective: To investigate the characteristics, outcomes, and follow-up of geriatric patients with do-not-resuscitate (DNR) orders after receiving non-invasive ventilation (NIV) in the emergency room (ER) and to evaluate the feasibility of caring for these patients in general medical wards.
Patients and methods: This retrospective study was conducted from January 2017 to December 2019. Of 1841 patients who were diagnosed with acute respiratory failure (ARF) in our ER, 147 received NIV as a salvage treatment. Among them, 121 patients (81 patients with DNR) who were older than 65 years and admitted to general medical wards for further care were included in this study.
Results: Patients with DNR orders were older (83.5 ± 0.9 years vs. 77.6 ± 1.3 years, $p < 0.01$) and had lower coma scale scores (10.7 ± 0.5 vs. 13.5 ± 0.5, $p < 0.01$), higher APACHE II scores (23.9 ± 0.8 vs. 20.7 ± 0.9, $p = 0.01$), and higher comorbidity scores (7.3 ± 0.2 vs. 6.5 ± 0.4, $p = 0.03$) than those without DNR orders. However, there were no differences in the causes of ARF between patients with and without DNR orders ($p = 0.74$). Patients with DNR orders had worse weaning outcomes (64.2% vs. 90%, $p < 0.01$) and hospital survival rate (61.7% vs. 90%, $p < 0.01$) than those without DNR orders. At 180 days after hospital discharge, 61.3% patients in the DNR group and 86.7% patients in the no DNR group were still alive ($p < 0.01$).
Conclusion: Patients with DNR orders were older and had more severe diseases, higher comorbidity, less consciousness, and worse weaning outcomes and hospital survival than those without DNR orders. Patients with DNR orders had a dismal prognosis even after hospital discharge.

1. Introduction

Acute respiratory failure (ARF) is a major cause of hospital visit. In recent years, the incidence of hospitalization for ARF has increased, especially in patients older than 65 years.[1,2] Mechanical ventilation (MV) has been used as a resolution for ARF. With the advancement of technique and knowledge, non-invasive mechanical ventilation (NIV) rather than invasive mechanical ventilation (IMV) has been used in several situations, including chronic obstructive pulmonary disease (COPD), congestive heart failure (CHF), and acute cardiogenic pulmonary edema.[3]

Wilson et al. reported that one in four patients with ARF had a do-not-intubate (DNI) order.[4] Although the rate of DNI orders varied across studies and geographical areas, the DNI rate had increased over time. DNI orders have an impact on the use of NIV. According to Bourke et al., NIV should not be used when it is very unlikely to succeed or when a purely palliative approach would be more appropriate.[3] However, Kacmarek suggested that the use of NIV in patients with DNI orders was practicable after receiving informed consent.[5]

Taiwanese population has been aging since 2018, and Taiwan will become a super-aged society by 2026.[6] In 2015, Taiwan passed a law entitled the Patient Autonomy Act, which states that a patient may decline medical treatment according to his/her will.[7] Since then, advance directives have become popular among elderly people and people with critical disease.[8] Elderly people are at a higher risk of various chronic diseases, such as COPD and CHF, than the other age groups.[9] Under such circumstance, we believed there were more elderly patients receiving NIV while facing ARF because of do-not-resuscitate (DNR) state. Several places such as intensive care units, general wards, and step-down units have been proposed for providing NIV.[10] In intensive care units, patients are monitored maximally, but stay in intensive care units is very costly for stable patients receiving NIV. Age is also a decisive factor for intensive care unit admission.[11] Moreover, many physicians were reluctant to admit geriatric patients in intensive care units.[12] Caring for stable patients receiving NIV in general wards would be more suitable and more efficient use of resources. However, the lack of caring skills might be a problem. In this study, we aimed to investigate the outcome of geriatric patients with DNR orders who received NIV in the emergency room (ER) and received subsequent care in general medical wards. Based on these results, we also aimed to explore the feasibility of caring for geriatric DNR patients in general wards.

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2. Methods

MacKay Memorial Hospital Tamsui Branch is a 950-bed tertiary hospital located in the northern part of New Taipei City. Annually, 58000 patients visit the ER in this hospital. Among them, on average, 600 patients are diagnosed with ARF in the ER. Data were collected retrospectively for all patients aged 65 years and older who were diagnosed with ARF in the ER between January 1, 2017, and December 31, 2019. All patients should receive bi-level pressure support (BIPAP) for NIV as a salvage therapy in the ER. After management in the ER, all these included patients were admitted to general medical wards. Patients were divided into two groups according to their DNR status. Moreover, DNR order should be acquired before the use of NIV. There were seven major causes of ARF: pneumonia, COPD, CHF, sepsis, uremic complications, cancer, and others. Basic characteristics, such as age, sex, length of hospital stay, and duration of ventilator use, were analyzed. The Acute Physiology and Chronic Health Evaluation II (APACHE II) score and modified Charlson comorbidity score were used to investigate disease severity and previous healthy status Glasgow coma scale was used to evaluate patients' mental status. Informed consent was waived by the Institutional Review Board of MacKay Memorial Hospital. The primary purpose of this study was to investigate the outcomes of NIV usage among geriatric patients with DNR orders. The secondary purpose of this study was to investigate the long-term outcomes of these patients after hospital discharge.

2.1. Statistical analysis

Categorical variables are expressed as number and percentage, and continuous data are expressed as mean ± standard deviation. All data were analyzed using Prism 5.0 software for Windows (GraphPad Software, Inc., La Jolla, CA, USA). Two-tailed Student's t-test was used to evaluate statistical significance. Kaplan-Meier survival curves were used to demonstrate survival over a follow-up period of 180 days, and the log-rank test was used for survival analyses. A p value less than 0.05 was considered statistically significant.

3. Results

During the study period, total 1841 patients were diagnosed with ARF in our ER. Among them, 147 patients received BIPAP for respiratory support. Of 147 patients, 121 were older than 65 years (Figure 1). There were 81 patients with DNR orders (66.9%, Table 1). Patients with DNR orders were older (83.5 ± 0.9 years vs. 77.6 ± 1.3 years, $p < 0.01$) and had lower coma scale scores (10.7 ± 0.5 vs. 13.5 ± 0.5, $p < 0.01$), higher APACHE II scores (23.9 ± 0.8 vs. 20.7 ± 0.9, $p = 0.01$), and higher comorbidity scores (7.3 ± 0.2 vs. 6.5 ± 0.4, $p = 0.03$) than those without DNR orders. There were no differences in the causes of ARF ($p = 0.74$), PaO_2/FiO_2 ratio ($p = 0.58$), renal function, and electrolyte level between patients with and without DNR orders. However, patients without DNR orders had a higher albumin level than those without DNR orders ($p < 0.01$).

We observed no difference in the duration of NIV use between patients with and without DNR orders (9.6 days vs. 6.6 days, $p = 0.16$, Table 2). However, at hospital discharge, patients with DNR orders had worse weaning outcomes compared to those without DNR orders (64.2% vs. 90%, $p < 0.01$, Table 2). There was no difference between the patients with and without DNR orders in terms of the duration of hospital stay (16.8 ± 1.2 days vs. 14.8 ± 2.5 days, $p = 0.41$, Table 2). However, the 21-day survival rate in patients with DNR orders was lower than that in patients without DNR orders ($p = 0.02$, Figure 2). The survival rate at hospital discharge was also worse in patients with DNR orders than that in patients without DNR orders (50 patients, 61.7% vs. 36 patients, 90%; $p < 0.01$; Table 2).

After hospital discharge, 44 patients in the DNR group and 30 patients in the no DNR group were available for follow-up. After 180 days follow-up, 27 patients (61.3%) in the DNR group and 26 patients (86.7%) in the no DNR group survived ($p < 0.01$, Figure 3).

4. Discussion

In 2000, Taiwan passed the Hospice Palliative Care Act, which enshrined patients' right to choose hospice and palliative care as well as established their right to sign DNR orders. Since then, the concept of hospice and palliative care has developed in Taiwan. Huang et al. reported that 77% of terminally ill patients had DNR orders in Taiwan.[13] Cheng et al. reported that 23% of patients had DNR orders while they visited the ER.[14] Our results showed that 69.4% of geriatric patients who received NIV had DNR orders. Three types of patients receive NIV: i) those who want to receive all possible treat-

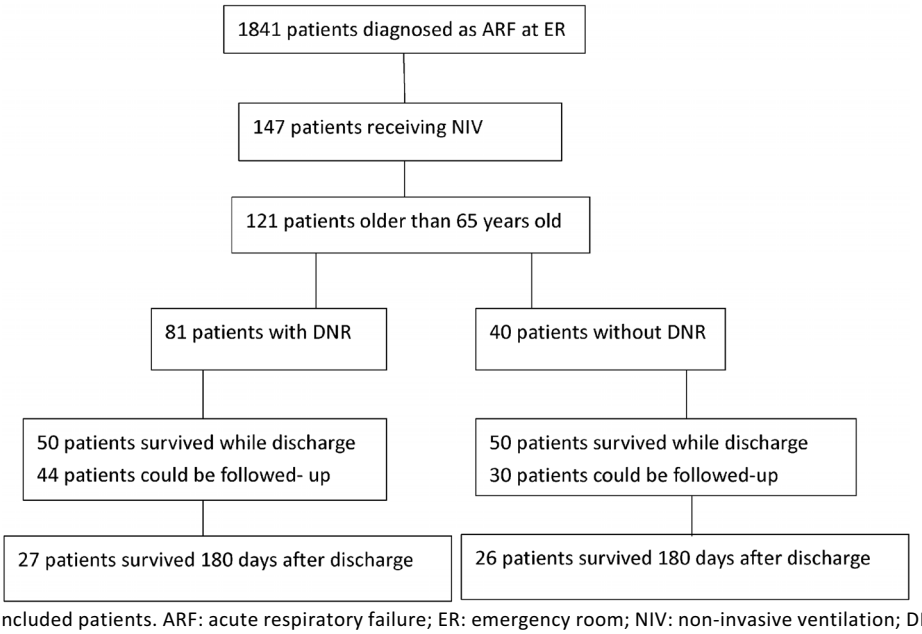

Figure 1. Flowchart for included patients. ARF: acute respiratory failure; ER: emergency room; NIV: non-invasive ventilation; DNR: do-not-resuscitate.

Table 1
Comparison between patients with and without do-not-resuscitate orders.

	Patients with DNR orders	Patients without DNR orders	p value
Number of patients (male patients)	81 (32)	40 (20)	0.28
Age, years	83.5 ± 0.9	77.6 ± 1.3	< 0.01
Glasgow coma scale score	10.7 ± 0.5	13.5 ± 0.5	< 0.01
APACHE II score	23.9 ± 0.8	20.7 ± 0.9	0.01
Charlson comorbidity score	7.3 ± 0.2	6.5 ± 0.4	0.03
Causes of acute respiratory failure, n			0.74
Chronic obstructive pulmonary disease	15	18	
Pneumonia	21	4	
Congestive heart failure	21	13	
Uremia	4	2	
Cancer	12	0	
Sepsis	4	0	
Others	4	3	
PaO_2/FiO_2 ratio	222.0 ± 16.8	239.0 ± 29.1	0.58
BUN, mg/dL	34.1 ± 3.1	25.5 ± 2.9	0.08
Creatinine, mg/dL	1.6 ± 0.2	1.5 ± 0.2	0.71
Sodium, mEq/L	132 ± 0.5	137 ± 0.7	0.16
Potassium, mEq/L	5.5 ± 1.2	4.1 ± 0.1	0.40
Albumin, g/L	3.3 ± 0.1	3.7 ± 0.1	< 0.01
Vasopressor use, n (%)	4 (4.9%)	1 (2.5%)	0.53

APACHE II: Acute Physiology and Chronic Health Evaluation II; BUN: blood urea nitrogen; DNR: do-not-resuscitate.
Data are presented as mean ± standard deviation.

Table 2
Hospital and NIV outcome of included patients.

Patient group	Patients with DNR	Patients without DNR	p valve
NIV duration (days)	9.6 ± 1.2	6.6 ± 1.9	0.16
NIV weaning			< 0.01
Case number (%)	52 (64.2%)	36 (90%)	
Hospital duration (days)	16.8 ± 1.2	14.8 ± 2.5	0.41
Hospital outcome			< 0.01
Survival cases (%)	50 (61.7%)	36 (90%)	

NIV: non-invasive ventilation; DNR: do-not-resuscitate.
Data are presented as mean ± standard deviation.

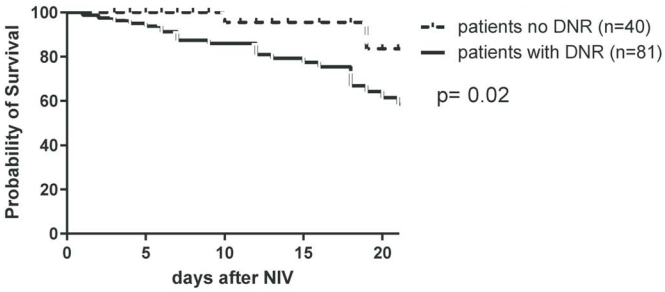

Figure 2. Kaplan-Meier estimates of the cumulative probability of survival after the use of Non- invasive ventilation for patients older than 65 years in the hospital. Those with DNR status had lower probability for 21 days' survival rate while comparing to those without DNR. DNR: do-not-resuscitate.

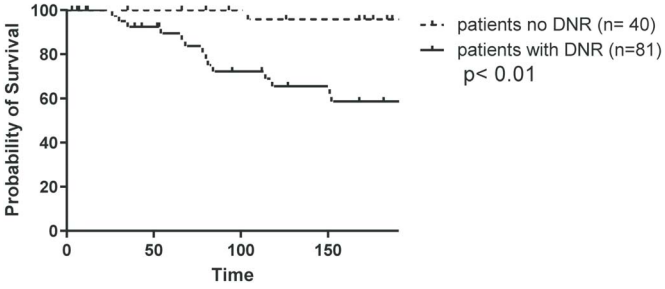

Figure 3. Kaplan-Meier estimates of the cumulative probability of survival after discharge up to 180 days. Those with DNR status had lower probability for survival while comparing to those without DNR. DNR: do-not-resuscitate.

ments and life support, ii) those who have special selection on life support and treatments (such as DNI/DNR orders), and iii) dying patients who wish to receive comfort measures only. In this study, patients with DNR orders were older and had lower coma scale scores, higher disease severity, and higher comorbidity scores than those without DNR orders. These findings are compatible with those reported by Chu et al.[8] With increasing age and severity of critical disease, the number of patients with DNR orders has been increasing.[8] Moreover, data from a Dutch geriatric ward showed that older patients with poor prognosis and a higher morbidity index were more likely to have DNR orders. Meanwhile, Cabrerizo et al. reported albumin as a prognostic factor for mortality in elderly people.[15] A low albumin level indicated a significant muscle loss, and it was associated with delayed recovery from acute pathologies. In this study, patients with DNR orders had a lower albumin level than those without DNR orders, indicating that patients with DNR orders might be more fragile and need more help for their activities of daily living due to their chronic diseases than those without DNR orders. In this study, older patients with high comorbidity and more critical conditions were more likely to have DNR orders might be because of their terminal conditions and the implementation of the Hospice Palliative Care Act in Taiwan. And we believe that most patients with DNR orders receiving NIV wished to receive comfort measures only.

In this study, there was no significant difference in the duration of NIV use between patients with and without DNR orders; the average duration of NIV use was 6.6 days in patients without DNR orders and 9.6 days in patients with DNR orders. The duration of NIV use varies across studies and ranges from less than 1 day to more than 30 days due to the difference in diseases and protocols used.[16–21] In our heterogeneous patient population, the causes of ARF varied. As mentioned above, most patients with DNR orders wished to receive comfort measures only, and they received NIV for a short duration before passing away. This might have contributed to the pooled analysis of the duration of NIV use and led to no difference in the duration of NIV use between patients with and without DNR orders.

According to previous studies, the weaning rate from NIV could vary from 56% to more than 80%.[16,18,19] Thille et al. showed that NIV

failure was associated with a lower Glasgow coma scale score.[22] Corrêa et al. also showed that elderly patients with a higher APACHE II score had a higher NIV failure rate.[23] In the present study, patients with DNR orders were older and had higher APACHE II scores and lower coma scale scores than those without DNR orders. This might explain the poor weaning outcomes in patients with DNR orders.

In a previous Taiwanese study, patients who were started on NIV in the ER had a mortality rate of 48%.[24] Vilaça et al. reported a survival rate of 49% in patients with DNI orders who received NIV as a salvage therapy in the ER.[25] In a meta-analysis of NIV use in patients with DNR orders by Wilson et al., the hospital survival rate and one-year survival rate after discharge were 56% and 32%, respectively.[26] In our study, a similar survival rate at discharge (61.7%) was observed in patients with DNR orders. Some studies have shown that patients with DNR orders had a poor hospital survival rate and long hospital stay if there was a delay in intubation after NIV failure.[23,24] However, in this study, patients with DNR orders did not have a chance of receiving intubation or even IMV as a salvage therapy because of their DNR state. This might have led to a high mortality rate in patients with DNR orders.

In our study, 53 patients (71.6%) survived after 180 days follow-up. Akyil et al. reported a mean survival duration of 27 months and asix-month mortality rate of 19.5% in patients with COPD after receiving NIV.[27] However, our results were similar to those reported by Chung et al.[28] They reported that the first-year survival rate was 72% in patients who received NIV. And Akyil et al. reported that old age and high Charlson comorbidity score had an impact on long-term survival in their patients. In this study, patients with DNR orders were older and had higher comorbidity scores compared to those without DNR orders. This might be the reason for the worse long-term outcomes in patients with DNR orders.

In our study, patients with DNR orders were older and had more severe diseases, higher comorbidity, lower coma scale scores, and worse weaning outcomes and hospital survival than those without DNR orders. Moreover, patients with DNR orders had dismal prognosis even after hospital discharge. However, our study has some limitations. First, it was a single-center, retrospective study. Therefore, there might be a bias in NIV usage. Second, this study was based on data from patients who received NIV and did not include patients who received IMV or high flow nasal cannula. Therefore, our results cannot generalized for all geriatric patients with ARF, a large multicenter prospective study is needed for further investigation.

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