

Clinical Experience of Noninvasive Positive Pressure Ventilation in Patients with Acute Cardiogenic Pulmonary Oedema Treated in a Community Hospital in Japan

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Abstract

Objective: To review our use of non-invasive positive pressure ventilation (NPPV) for acute cardiogenic pulmonary oedema (ACPO) in the routine clinical management, especially in terms of the timing of endotracheal intubation (ETI) and outcome.

Methods: We retrospectively reviewed 61 patients diagnosed with ACPO admitted to our emergency room (ER) or intensive care unit (ICU) and who received NPPV. The reasons for ETI were reviewed, and the intervals between the estimated appropriate time for ETI and the actual time of ETI and in-hospital mortality were recorded.

Results: The mortality rate of patients receiving NPPV was 8.2% (five out of 61). Forty-eight patients (78.7%) were successfully weaned off NPPV without ETI, and 13 (21.3%) required ETI. Five of the 13 intubated patients died, but there was no significant difference in the duration of NPPV before ETI between those who survived and those who died. The interval between the estimated appropriate time for ETI and the actual time of ETI was significantly shorter in patients who survived than in those who died (1.9 ± 3.8 hours versus 8.6 ± 5.4 hours, $p=0.02$). The mortality rate was significantly higher in patients with an interval of longer than 1.8 hours between the estimated appropriate time for ETI and the actual time of ETI (66.7% versus 14.3%, $p<0.001$).

Conclusions: In patients with ACPO receiving NPPV, a delay in performing ETI beyond the appropriate time was significantly associated with increased mortality. The duration of NPPV before ETI was not associated with mortality.

Keywords: Intensive care unit; Emergency room; Acute cardiogenic pulmonary oedema; Noninvasive positive pressure ventilation; Endotracheal intubation; Community hospital.

Abbreviations

NPPV=Non-invasive positive pressure ventilation; ACPO=Acute cardiogenic pulmonary oedema, ETI=Endotracheal intubation; ER=Emergency room; ICU=Intensive care unit; CPAP=Continuous positive airway pressure; BiPAP=Bi-level positive airway pressure; COPD=Chronic obstructive pulmonary disease; ARF=Acute respiratory failure; ABG=Arterial blood gas; SpO₂=Peripheral oxygen saturation; FiO₂=Inspired oxygen fraction; PEEP=Positive end expiratory pressure; APACHE=Acute Physiology and Chronic Health Evaluation.

Introduction

Continuous positive airway pressure (CPAP) or bi-level positive airway pressure (BiPAP) ventilation, collectively termed non-invasive

positive pressure ventilation (NPPV), appear to be effective means of reducing the rates of endotracheal intubation (ETI) and morbidity and mortality when treating patients with acute cardiogenic pulmonary oedema (ACPO) [1-3]. NPPV is increasingly used to treat ACPO in combination with standard pharmacological treatments; however, there have been recent reports that patients who receive NPPV in routine clinical practice may have much poorer outcomes than those enrolled in randomized controlled trials, in which patients are more carefully selected and may receive more intensive care and monitoring [4-9]. Furthermore, some studies have reported high mortality rates in the small group of patients with chronic obstructive pulmonary disease (COPD) who had an initial successful response to NPPV but subsequently required mechanical ventilation because of a second episode of acute respiratory failure (ARF) [6,10,11]. Although the proportion of patients requiring mechanical ventilation because of a second episode of ARF has remained stable, the absolute number of patients receiving NPPV has increased over time because of the increased availability of the technique [6]. The increased use of NPPV in diverse populations with ARF has been associated with increased in-hospital mortality rates, probably because of delays in performing ETI

[12,13]. These reports indicate that patients with a second episode of ARF after an initial successful response to NPPV may be at particularly high risk. These general themes may also be important when considering the management of critically ill patients with ACPO.

The objective of this retrospective cohort study was to review our use of NPPV in the routine clinical management of ACPO in terms of the timing of ETI and outcome.

Materials and Methods

Conduct of the study was approved by the Ethics Review Board of Shinbeppu Hospital. The requirements for informed consent were waived as clinical data, but none that could identify a patient, were collected retrospectively from the medical records alone. The study protocol did not include any protocol-specified treatment alteration and our patient record system was designed to enable anonymized clinical data to be collected for research.

Study population

We retrospectively examined the medical records of 86 patients treated for ACPO in the emergency room (ER) or intensive care unit (ICU) of Shinbeppu Hospital, Japan, between January 2009 and June 2012 and who received NPPV. NPPV was not used in patients who required immediate ETI, or who were in respiratory or cardiac arrest at the time of admission. Patients with a reduced level of consciousness (Glasgow Coma Scale score <10), acute ST-segment elevation myocardial infarction and pneumonia have often been excluded from previous studies [14,15], but were included in this study.

Initial management

Patients presenting to the ER with ACPO were initially treated with supplemental oxygen at 5–10 L/min via (reservoir) facemask and in most cases with a bolus of 20 mg intravenous furosemide until a physician with expertise in cardiology could attend. The decision to initiate NPPV was made after the attending cardiologist (or the duty ER physician, if they had cardiology expertise) confirmed the diagnosis of ACPO. Inpatients who developed ACPO while on a general ward were given NPPV in that ward or after transfer to the ICU. Use of NPPV did not alter or restrict pharmacological treatments. Staffing issues meant that arterial blood gas (ABG) analysis could not always be undertaken; therefore we used peripheral oxygen saturation (SpO₂) to evaluate the response to treatment.

A Servo-i or Servo-s ventilator (Siemens-Elema, Uppsala, Sweden) was employed for NPPV, connected to a ComfortGel Blue full-face mask (Philips Respironics, Amsterdam, Netherlands) or a Caster helmet (Starmed, Mirandola, Italy). The initial inspired oxygen fraction (FiO₂) was 1.0 in most cases. Selection of CPAP or BiPAP was at the discretion of the attending cardiologist. CPAP was selected in most cases, and the positive end expiratory pressure (PEEP) was initially set at 5 cm H₂O, but was increased to 10 cm H₂O if needed, depending on the clinical response and tolerability for the patient. When BiPAP was selected, inspiratory positive airway pressure was initially set at 10 cm H₂O and PEEP was set at 5 cm H₂O. When a helmet was used, inspiratory positive airway pressure was initially set at 15 cm H₂O and PEEP was set at 10cm H₂O. In almost all cases, no further changes in ventilator settings were made in the ER. After stabilization, the patient was transferred to the ICU and NPPV was continued.

Management in the ICU

After admission to the ICU, the electrocardiogram, SpO₂, respiratory rate, and heart rate were monitored continuously; and arterial blood pressure, body temperature, and urine output were monitored intermittently. As oxygen had often been delivered using variable performance devices before NPPV was initiated, it was not possible to determine FiO₂ on admission reliably. We therefore analysed PaO₂ on admission rather than the PaO₂/FiO₂ ratio. Based on the instructions of the attending physician, the FiO₂ was gradually reduced by the nursing staff to maintain the SpO₂ above 90–95%. Patient management did not follow any specific protocol, and decisions to discontinue NPPV or intubate the trachea were made by the attending physician. Weaning was considered successful if NPPV was not resumed within 48 hours of discontinuation [16]. Chest radiographs and routine blood tests were requested at the time of admission to the ER or ICU by the attending cardiologist.

Timing of ETI

The period of NPPV before ETI was reviewed in all patients. Previous studies have used different criteria for the timing of ETI in patients receiving NPPV (Supplementary Table 1) [14,15,17-20]. We determined the appropriate time for ETI based on the most commonly reported criteria: 1) cardiac or respiratory arrest; 2) refractory hypoxemia despite maximal therapy; 3) deterioration of the level of consciousness; 4) inability to improve dyspnoea and ABG parameters within 1 hour; 5) haemodynamic instability; 6) life-threatening ventricular arrhythmia; 7) psychomotor agitation; 8) inability to tolerate the face mask; 9) the decision of the attending cardiologist; and 10) when NPPV had been used as a temporizing measure to avoid ETI while initiating definitive therapy but gas exchange had deteriorated after an initial improvement [2,21-23].

	Non-ETI patients (n=48)	ETI patients (n=13)	Survived after ETI (n=8)	Deceased after ETI (n=5)
Age (years)	76.8 ± 10.4	73.7 ± 7.1	72.9 ± 8.0	75.0 ± 6.2
Male/female	29/19	9/4	6/2	3/2
APACHE II score	17.5 ± 5.3 (n=43)	22.0 ± 5.0	21.1 ± 4.4	23.4 ± 6.2
Pneumonia severity index	170.3 ± 34.7	185.3 ± 33.8	183.7 ± 15.8	186.5 ± 46.0
Cause of ACPO				
Hypertensive heart disease	9			
Arrhythmia	2	1		1
Ischemic heart disease (including AMI)	25	8	5	3
Valvular heart disease	6	2	2	
Cardiomyopathy	5	1	1	
Others	1	1		1
Comorbidities				

Hypertension	19	6	4	2
Coronary artery disease	30	8	6	2
Peripheral artery disease	5	1	1	
Cerebrovascular disease	9	4	3	1
Atrial fibrillation	10	3	2	1
Valvular heart disease	6	2	2	
Bacterial pneumonia	12	8	4	4
Diabetes mellitus	22	4	4	
Hyperlipidemia	12	5	3	2
Renal dysfunction	26	5	3	2
Anaemia	38	10	7	3
Hepatic disease	5	1		1
Respiratory disease	2	2	1	1
Cognitive dysfunction	4	3	2	1
Cancer	3	1		1

Table 1: Baseline clinical characteristics of patients. Values are the mean ± standard deviation or number of patients (number of patients with complete or partial information available in the medical records).

Abbreviations: ETI: Endotracheal Intubation; APACHE: Acute Physiology and Chronic Health Evaluation; ACPO: Acute Cardiogenic Pulmonary Oedema; AMI: Acute Myocardial Infarction.

Statistical analysis

We undertook a power analysis to calculate the required sample size for our study. To inform this calculation, we used an estimated mortality rate of 91.7% for patients intubated at an inappropriate time [10] and 15.4% for patients intubated at an appropriate time [2]. Consequently, the power calculation suggested that a sample size of 5 patients in each group would be needed to detect a statistically significant difference (alpha-error 0.05, power 0.8).

Data are presented as the mean ± standard deviation. The unpaired Student's t-test was used to compare variables. The χ^2 test was used to examine differences in mortality rates between groups. Microsoft Excel was used for statistical analyses. A p value of less than 0.05 was considered statistically significant.

Results

Patient characteristics

A schematic diagram of the patient recruitment process is shown in Figure 1. Between January 2009 and June 2012, 115 patients with suspected ACPO were admitted to our ER/ICU. Fifty-four patients

(47.0%) were excluded because they did not meet the inclusion or exclusion criteria for the following reasons: 29 required conventional oxygen therapy or immediate ETI, four were misdiagnosed, two were treated using NPPV ventilators that were not designed for ICU use, eight either had do-not-ETI orders or advance directives, one had insufficient data entered in the medical records, one patient discontinued NPPV unexpectedly for emergency cardiac catheterization, two received on-going NPPV despite further deterioration in conscious level, two had terminal cancer, one was intubated for surgery, three were intubated due to sudden unexpected exacerbation of respiratory distress after successful weaning from NPPV and one had to be administered NPPV as ETI could not be achieved. Ultimately, the data of 61 patients were analyzed (Figure 1).

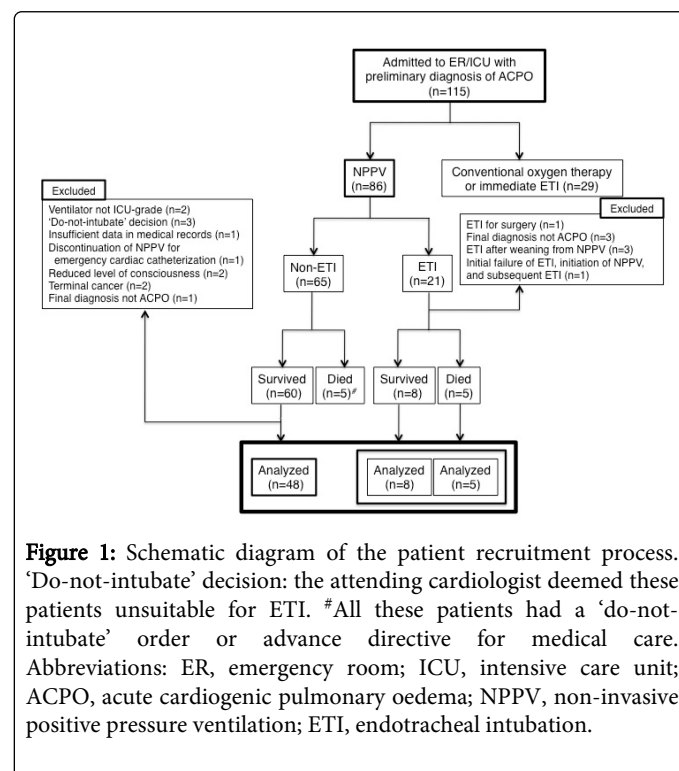


Figure 1: Schematic diagram of the patient recruitment process. 'Do-not-intubate' decision: the attending cardiologist deemed these patients unsuitable for ETI. #All these patients had a 'do-not-intubate' order or advance directive for medical care. Abbreviations: ER, emergency room; ICU, intensive care unit; ACPO, acute cardiogenic pulmonary oedema; NPPV, non-invasive positive pressure ventilation; ETI, endotracheal intubation.

Thirteen of the 61 patients (21.3%) were intubated. Of the 48 patients who received NPPV but did not require intubation, none died and all were discharged from hospital. Five out of the 13 patients requiring ETI died (38.5%). The in-hospital mortality rate of the entire cohort was 8.2% (five out of 61).

The clinical and demographic characteristics of the patients, causes of ACPO and comorbidities are shown in (Table 1). None of the intubated patients had ACPO caused by hypertensive heart disease (hypertensive crisis), which arguably would have been better treated with NPPV anyway. All patients had multiple comorbidities.

There were significant differences in the mean Acute Physiology and Chronic Health Evaluation (APACHE) II score in those who underwent ETI (ETI patients) whose scores averaged $22.0 \pm$ standard deviation 5.0, compared with those who did not undergo ETI (non-ETI patients, Table 1; $p=0.008$), whose scores averaged $17.5 \pm$ 5.3. However, there were no significant differences between ETI patients who survived and ETI patients who died (Table 1, $p=0.45$). There were also no significant differences in the pneumonia severity index

between ETI patients and non-ETI patients ($p=0.37$), and between ETI patients who survived and ETI patients who died ($p=0.92$).

Response to NPPV

The responses to NPPV in all patients are shown in Table 2. The PaCO₂ was significantly lower at the time of initial lowering of FiO₂ ($p=0.02$) and at the time of weaning from NPPV ($p=0.002$) than at

admission. Non-ETI patients had a persistently high PaO₂/FiO₂ ratio throughout the duration of NPPV that had not changed significantly by the time of weaning ($p=0.49$). No patients in this group required a subsequent increase in FiO₂ to maintain SpO₂ after the initial lowering of FiO₂. The mean time from the initiation of NPPV to the first lowering of FiO₂ was 1.5 ± 1.9 hours and mean duration of NPPV was 22.9 ± 17.6 hours.

	Non-ETI patients (n=48)	ETI-Patients (n=13)		P value#
		Survivors (n=8)	Deceased (n=5)	
Respiratory rate on admission (min⁻¹)	29.2 ± 7.0 (n=30)	32 ± 8 (n=8)	32 ± 7 (n=3)	0.93
PaO₂ on admission (mmHg)	87.7 ± 26.8 (n=28)	65.3 ± 13.4 (n=5)	80.3 ± 24.8 (n=4)	0.28
PaCO₂ (mmHg)				
on admission	49.2 ± 12.7 (n=30)	45.2 ± 12.8 (n=5)	36.7 ± 3.3 (n=4)	0.24
at time of initial lowering of FiO ₂	41.9 ± 7.5 (n=23)*	28.6	48.0 ± 30.2 (n=3)	
at time of weaning from NPPV	37.6 ± 5.9(n=15)**			
at time of ETI		67.5 ± 12.2 (n=2)	38.2 ± 13.5 (n=2)	0.15
after ETI		39.0 ± 8.1 (n=8)	46.9 ± 19.6 (n=5)	0.33
FiO₂				
initial	0.9 ± 0.2 (n=48)	1.0 ± 0.1 (n=8)	0.9 ± 0.2 (n=5)	0.19
at time of weaning from NPPV	0.4 ± 0.1 (n=48)			
at time of ETI		0.9 ± 0.2 (n=8)	0.8 ± 0.2 (n=5)	0.29
could not be lowered	0	6 patients	1 patient	
PaO₂/FiO₂				
at time of initial lowering of FiO ₂	374 ± 118 (n=23)	297 (n=1)	258 ± 109 (n=3)	
at time of weaning from NPPV	348 ± 103 (n=15)			
at time of ETI		109 ± 74 (n=2)	234 ± 167 (n=2)	0.44
after ETI		240 ± 104 (n=8)	190 ± 94 (n=4)	0.44
Latency (hours)				
to initial lowering of FiO ₂	1.5 ± 1.9 (n=43)	0.3 ± 0.3 (n=2)	1.6 ± 1.3 (n=4)	0.24
to weaning from NPPV	22.9 ± 17.6 (n=48)			
to ETI		3.8 ± 4.7 (n=8)	15.0 ± 16.0 (n=5)	0.09
between timing of the estimated appropriate time for ETI and the actual time of ETI		1.9 ± 3.8 (n=8)	8.6 ± 5.4 (n=5)	0.02
Increasing FiO₂ during NPPV (n)	0	1 patient	2 patients	

Table 2: Responses to NPPV. Values are the mean ± standard deviation or the number of patients (number of patients with complete or partial information available in the medical records). * $p=0.02$, ** $p=0.002$, compared with the value at admission. # comparisons between surviving and deceased patients.

Abbreviations: NPPV: Noninvasive Positive Pressure Ventilation; PaO₂: Arterial partial pressure of oxygen; PaCO₂: Arterial Partial Pressure of Carbon dioxide; FiO₂: Fraction of Inspired Oxygen; ETI: Endotracheal Intubation.

Endotracheal intubation was performed under emergency circumstances in most cases (Supplementary Table 2-1), and there was limited time available for ABG analysis. Unlike the non-ETI patients, the ETI patients did not show sustained improvement in PaCO₂.

Furthermore, the FiO_2 could not be lowered in seven of these patients (patients 2, 4, 5, 6, 7 and 8 of the surviving ETI group and patient 2 of the deceased ETI group) and the FiO_2 needed to be increased again after initial lowering to maintain SpO_2 above 90–95% in three patients (patient 3 of the surviving ETI group and patients 1 and 3 of the deceased ETI group).

Reasons for ETI

Five of the eight surviving patients who underwent ETI were intubated within 1 hour of initiation of NPPV (Supplementary Table 2-1), as a result of their poor clinical condition on admission. The other three surviving ETI patients were intubated as a consequence of deterioration in their clinical condition during NPPV. Of the five deceased ETI patients, four underwent ETI because of deterioration in their clinical condition during NPPV. The remaining patient developed an acute exacerbation of respiratory distress in the general ward, for which he initially received NPPV. After transfer to the ICU, he was noted to have frothy pink sputum when coughing, and he underwent ETI.

Estimated appropriate time for ETI and patient outcome

There was no significant difference in the time that elapsed from the initiation of NPPV to ETI between the surviving ETI patients and the deceased ETI patients (3.8 ± 4.7 hours versus 15.0 ± 16.0 hours, $p=0.09$; Table 2). However, the interval between the estimated appropriate time for ETI and the actual time of ETI was significantly shorter in the surviving ETI patients than in the deceased ETI patients (1.9 ± 3.8 hours versus 8.6 ± 5.4 hours, $p=0.02$; Table 2). The estimated appropriate time for ETI concurred with the actual time of ETI in six patients (Supplementary Table 2-2), five of whom survived and one of whom died. Three patients survived and four died when there was a difference between the estimated appropriate time and the actual time of intubation. The median interval from the estimated appropriate time for ETI and the actual time of ETI was 1.8 hours. The in-hospital mortality was 66.7% if delay in intubation after the time that ETI was deemed appropriate exceeded 1.8 hours, compared with 14.3% if the delay was less than 1.8 hours ($p<0.001$; Table 3).

	Deceased	Survived	Total	Mortality
Delay group	4	2	6	66.7%
Non-delay group	1	6	7	14.3%
Total	5	8	13	$P<0.001$

Table 3: Clinical outcome and interval between the estimated appropriate time for ETI and the actual time of ETI. Values are the number of patients. Delay group: interval between the estimated appropriate time for ETI and the actual time of ETI exceeded the median (1.8 h).

Abbreviations: ETI: endotracheal intubation.

Discussion

We found that delay in ETI after the time that ETI is deemed appropriate was associated with a significant increase in mortality, but not the duration of NPPV before ETI. Even though the ETI rate (21.3%) and overall in-hospital mortality rate (27.2%) of patients who

received NPPV in this study are higher than the rates reported in clinical trials, our results compare favourably with those of other similar observational studies [5,9,12]. We therefore believe that the findings of this study reflect the realities of using NPPV in routine clinical practice.

NPPV is a supportive treatment that aims to buy sufficient time for definitive therapy such as vasodilatation or diuresis to be established, and thus avoid the need for ETI [2,21-23]. Emergency ETI in hypoxic, critically ill, haemodynamically unstable patients is associated with high mortality rates, while patients with acute decompensated heart failure who receive NPPV appear to have significantly better outcomes [2,24]. The likelihood of a therapeutic response to NPPV can be predicted soon after its initiation. Those patients in whom ABG parameters and tachypnoea improve after a 60 min short-term trial (STT) of NPPV have better subsequent outcomes [2,17]. In our cohort, it is likely that patient 5 in the surviving ETI group and patients 3 and 5 in the deceased ETI group should have been intubated as soon as it became clear that the STT of NPPV had not been effective (Supplementary Tables 2-1 and 2-2, respectively).

Previous studies have used a wide range of criteria to help inform the decision to intubate a patient receiving NPPV (Supplementary Table 1); however, it is not clear whether these criteria still apply if a patient initially improves after initiation of NPPV but subsequently deteriorates. Patients who develop a second episode of ARF after an initial successful response to NPPV have a high mortality rate, particularly if NPPV is continued more aggressively and ETI avoided [6,10,11]. Our findings suggest that the two patients in whom oxygen requirements rose again after an initial improvement in gas exchange should have been intubated immediately, even though they were calm and not dyspnoeic (patient 3 in the surviving ETI group and patient 1 in the deceased ETI group). Patient 4 in the deceased ETI group had had an acute myocardial infarction, underwent emergency percutaneous coronary intervention (PCI) and were reliant upon intra-aortic balloon pumping. Although his tachypnoea improved and he became calmer after initiation of NPPV, a FiO_2 of 0.6 was needed to maintain his $\text{PaO}_2/\text{FiO}_2$ ratio above 300 for over 10 hours after the STT. In the context of a very high serum creatine phosphokinase concentration (11,202 IU/L 1 hour after PCI), it is a moot point as to whether ETI would have improved this patient's chance of survival. Nevertheless, this case highlights the difficulty of clinical decision-making in patients who neither deteriorate nor improve, or who improve very slowly.

We found that all patients included in the analysis had multiple comorbidities (Table 1), some of which are likely to have either accelerated the progression of heart failure or directly precipitated ACPO [25]. Moretti et al. [10] reported that a second episode of ARF was more likely to occur in patients with more severe functional limitation and clinical disease who had more complications at the time of ICU admission [10]. As treatment strategies for ACPO evolve, adequately addressing the contribution of comorbidities is gaining increasing importance [25]. The significant difference that we observed between the mean APACHE II score in ETI patients compared with non-ETI patients reflects the more severe and extensive comorbidities of those intubated. It has also been suggested that prolonged NPPV may be detrimental, and that ETI should not necessarily be avoided at all costs [18], as ETI addresses physiological deteriorations in diaphragmatic and pulmonary function, and has other benefits (for example enhancing cardiac function, decreasing systemic acidosis and improving delirium) [13,26]. For this reason, at

the time when an initial improvement in gas exchange appears to have plateaued, ETI and mechanical ventilation may bring benefits to comorbid conditions even if patient does not appear to be deteriorating.

There is no clear evidence on how long to persist with NPPV in a calm patient whose initial improvement in gas exchange appears to have plateaued. Clinical trials have not addressed these complex issues and would be very challenging to design and conduct. Patients with this extent of comorbidity would likely have been excluded from most clinical trials, and as a consequence it can be argued that the best available evidence only applies to the patients who would be most likely to respond to treatment anyway. The strength of our study is that it reflects routine clinical practice and can help inform day-to-day clinical decision-making.

The duration of NPPV is also an important factor in the decision to perform ETI and mechanical ventilation. Some clinical trials of NPPV in patients with ACPO reported a mean total duration of less than 10 h [19,20]. Our findings show that the duration of NPPV, if tolerated, did not influence in-hospital mortality, with a broadly comparable mean duration of treatment. A study of a similarly heterogeneous group of patients reported that those who eventually required ETI initially required significantly longer daily CPAP therapy than those who did not require ETI, but that CPAP did not reduce the need for ETI or improve the outcome after ETI [21]; notably, however, some participants in this study required ETI more than 10 days after study entry. The clinical courses of the non-ETI patients in our study provide insights into the ways that NPPV is routinely used, which cannot necessarily be obtained from randomized trials.

We have used our findings to inform the design of a protocol to help physicians determine the optimal timing of ETI and mechanical ventilation in patients with ACPO who are receiving NPPV. In addition to the criteria described above for discontinuation of NPPV and performance of ETI, our protocol recommends ETI in the following patients: 1) those in whom mechanical assistance such as intra-aortic balloon pumping or renal replacement therapy is needed during NPPV; 2) those in whom FiO_2 cannot be lowered within the first hour after initiation of NPPV; 3) those in whom the $\text{PaO}_2/\text{FiO}_2$ ratio fails to improve to 138 even with an FiO_2 of 1.0 within the first hour after initiation of NPPV; 4) those with persistent hypercapnia during the first hour after initiation of NPPV; 5) those in whom the FiO_2 was initially reduced but who need a subsequent increase in FiO_2 to maintain SpO_2 above 90–95%; 6) those who are considered difficult to wean from NPPV within 23 hours with an FiO_2 of 0.4 ± 0.1 ; and 7) those with a $\text{PaO}_2/\text{FiO}_2$ ratio of less than 348 with an FiO_2 of 0.4 ± 0.1 at the time of weaning from NPPV. All medical staff who administers NPPV must be vigilant to the fact that a patient may deteriorate even if they have initially responded to treatment supported by NPPV.

Our study has some limitations. First, the number of patients is relatively small and may have resulted in bias. Second, a retrospective observational study from a single centre cannot establish valid conclusions regarding the efficacy of our protocol. Third, ABG analysis was not performed regularly in all patients. It will be important to examine the effectiveness of our protocol in a future prospective trial.

Conclusion

The interval between the estimated appropriate time for ETI and the actual time of ETI was significantly shorter in surviving ETI

patients than in deceased ETI patients. Delays beyond the estimated appropriate time for ETI were significantly associated with a higher mortality rate, but in our cohort the duration of NPPV before ETI was not associated with mortality.

Authors contributions

EO conceived the study, participated in the study design and coordination, drafted the manuscript, and participated in the statistical analysis and interpretation of data. MY participated in study coordination. SS participated in study design and coordination, drafted the manuscript, and participated in statistical analysis and interpretation of data. TM, TK, KW, KK, DS, HO and NN participated in the design of the study. KA and KM participated in statistical analysis. All authors have read and approved the final manuscript.

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