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Original article

## Beneficial effects of rapid introduction of adaptive servo-ventilation in the emergency room in patients with acute cardiogenic pulmonary edema

Masaki Kinoshita (MD), Hideki Okayama (MD, FJCC)\*, Go Kawamura (MD), Tatsuya Shigematsu (MD), Tatsunori Takahashi (MD), Yoshitaka Kawata (MD), Go Hiasa (MD, FJCC), Tadakatsu Yamada (MD), Yukio Kazatani (MD, FJCC)

Department of Cardiology, Ehime Prefectural Central Hospital, Ehime, Japan

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### ABSTRACT

**Background:** Adaptive servo-ventilation (ASV) at home has been used for patients with chronic heart failure. However, its effect on acute cardiogenic pulmonary edema (ACPE) is not clear. The aim of this study was to elucidate the effect of ASV use in the emergency room in patients with ACPE.

**Methods:** We enrolled 198 consecutive patients with ACPE. Eighty patients received standard therapies, such as oxygen inhalation and vasodilators (conventional therapy group), and 118 received ASV in addition to standard therapy (ASV therapy group). ASV was initiated in the emergency room immediately after diagnosis. The procedure was switched over from ASV to endotracheal intubation (ETI) when oxygenation was insufficient.

**Results:** The ETI rate in the ASV therapy group was significantly lower than that in the conventional therapy group (3% vs. 21%,  $p < 0.01$ ). The intensive care unit and/or high care unit length of stay in the ASV therapy group was also significantly shorter than that in the conventional therapy group ( $1.9 \pm 2.1$  days vs.  $5.3 \pm 6.8$  days,  $p < 0.01$ ). Consequently, the hospitalization period in the ASV therapy group was shorter than that in the conventional therapy group ( $19.3 \pm 11.0$  days vs.  $26.3 \pm 16.6$  days,  $p < 0.01$ ).

**Conclusion:** In patients with ACPE, rapid introduction of ASV in the emergency room reduces the need for ETI and decreases the hospitalization period.

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### Introduction

Acute cardiogenic pulmonary edema (ACPE) is a common condition that can lead to high in-hospital mortality. Standard therapy for patients with ACPE includes medical treatment and respiratory management. Noninvasive positive pressure ventilation (NPPV) has been shown to improve pulmonary edema in patients with acute heart failure (AHF) [1–7]. Meta-analysis studies have also reported the effect of NPPV in patients with ACPE [8–12]. NPPV significantly decreases mortality and reduces the rate of endotracheal intubation (ETI) in these patients [8]. In the guidelines of the Japanese Circulation Society (JCS), NPPV is the first line of treatment for ACPE [1]. However, the Acute

Decompensated Heart Failure Syndromes (ATTEND) registry has demonstrated that the rate of NPPV use is only about 20% in patients with ACPE [13,14]. Since conventional, stationary-type NPPV machines require plumbing for oxygen and can only be used in the intensive care unit (ICU) or high care unit (HCU), the development of an innovative ventilator that could be used anywhere and was simple to operate was required. In line with this, adaptive servo-ventilation (ASV), a form of NPPV, has been used for patients with chronic heart failure (CHF) at home [15]. Patients can operate ASV at home because of its ease of use and compact size. In addition, since ASV does not need plumbing for oxygen, it can be used anywhere. In other words, ASV may be feasible for use in the emergency room, during transportation, and on general wards. This means that ASV can be used seamlessly from the hospital's door to the general ward, and occasionally at home. Furthermore, ASV is synchronized to the respiration patterns of individual patients by an original algorithm and adds pressure support. Thus far, there are few reports on ASV therapy for patients with ACPE [16]. Thus, the effects of ASV on

\* Corresponding author at: Department of Cardiology, Ehime Prefectural Central Hospital, 83 Kasuga-machi, Matsuyama, Ehime 790-0024, Japan.  
Tel.: +81 89 947 1111; fax: +81 89 943 4136.

E-mail address: [c-hokayama@eph.pref.ehime.jp](mailto:c-hokayama@eph.pref.ehime.jp) (H. Okayama).

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acute hemodynamic parameters and during the subsequent clinical course (i.e. intensive care unit stay, hospitalization period) are still unknown. The objective of this study was to elucidate the effect of rapid introduction of ASV in the emergency room in patients with ACPE.

## Materials and methods

Between April 2009 and December 2014, 277 patients with ACPE were admitted to the emergency room of Ehime Prefectural Central Hospital, Japan. All patients had a New York Heart Association (NYHA) functional class of either III or IV. Heart failure (HF) was diagnosed according to the Framingham criteria (satisfaction of 2 major criteria or 1 major and 2 minor criteria) [17]. ACPE was defined as: (1) acute HF or acute exacerbation of chronic HF; (2) presence of pulmonary edema shown by radiograph. When patients were admitted to the emergency room, initial treatment was performed according to the physician's judgment. Exclusion criteria were do not attempt resuscitation (DNAR) order, history of NPPV, cardiogenic shock, fatal arrhythmia, infection, acute coronary syndrome, disturbance of consciousness, or right-sided HF. Conventional therapy group received standard therapies, such as oxygen inhalation with a mask, gatch up (sitting position), diuretics, vasodilators, inotropic support, and ASV therapy group received ASV in addition to standard therapy, according to the attending physician's judgment. Data on the acute phase were determined before and 1 h after respiratory management.

The baseline characteristics of the patients including age, sex, NYHA functional class, new-onset HF, clinical scenario, and etiology of HF (e.g. ischemic or non-ischemic) were recorded. Past medical history (e.g. hypertension, diabetes mellitus, dyslipidemia, atrial fibrillation, and chronic kidney disease) was also archived. Hypertension, diabetes mellitus, and dyslipidemia were defined when patients were receiving drugs related to these conditions. We defined chronic kidney disease when the estimated glomerular filtration rate had been less than 60 ml/min/1.73 m<sup>2</sup> for 3 months. Left ventricular ejection fraction on admission was measured using a modified Simpson's method. Laboratory data including blood gases [e.g. pH and arterial partial pressure of O<sub>2</sub> (PaO<sub>2</sub>) and CO<sub>2</sub> (PaCO<sub>2</sub>)], serum creatinine concentration, and plasma brain natriuretic peptide were archived. Medications taken prior to admission including beta-blockers, angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, furosemide, spironolactone, and statins were also recorded.

The ventilator used for ASV therapy in our study was an advanced bi-level positive airway pressure unit (AutoSet CS™ or

ResMed, Sydney, Australia) with a full-face or total face mask [18]. ASV was initiated in the emergency room as soon as a diagnosis was made. The initial settings for ASV were an end-expiratory pressure (EEP) of 5–10 cmH<sub>2</sub>O, a minimum pressure support (PS) of 3 cmH<sub>2</sub>O, and a maximum PS of 10 cmH<sub>2</sub>O. ASV combined with a small battery was able to add continuous EEP even during transportation. A flow rate of oxygen through the port connector was regulated according to oxygen saturation (SaO<sub>2</sub>) improvement (greater than 95%). Fig. 1 shows the initial settings of ASV. Conventional or ASV therapy was switched over to ETI based on the attending physician's discretion, whenever oxygenation was insufficient. Immediate indication of ETI in emergency room was cardiogenic shock, fatal arrhythmia, or disturbance of consciousness. The rate of ETI and changes in vital signs during the acute phase were evaluated. Furthermore, ICU and/or HCU length of stay and hospitalization period, and in-hospital mortality were evaluated in both groups.

Data for continuous variables were expressed as mean ± standard deviation (SD). Data for continuous variables from the conventional therapy and ASV therapy groups were compared using Student's *t*-tests and two-way analysis of variance (ANOVA) with repeated measure followed by Scheffe's tests. Differences in proportions between the groups were calculated by the  $\chi^2$  test. A value of  $p < 0.05$  was considered statistically significant. All statistical analyses were performed using SPSS for Windows version 22.0 (SPSS, Chicago, IL, USA). The study was approved by the Ethics Committee of Ehime Prefectural Central Hospital (No. 26-45). All procedures were performed in accordance with the ethical standards of the responsible committee on human experimentation and the Helsinki Declaration of 1964.

## Results

A flowchart of the patient selection process is shown in Fig. 2. Ten patients received immediate ETI after physical examination in the emergency room. Sixty-nine patients were excluded in accordance with the exclusion criteria. Finally, we analyzed retrospectively 198 consecutive patients with ACPE (122 men, mean age: 74 ± 12 years). Eighty patients received standard therapies and 118 received ASV therapy. Table 1 shows the patients' baseline characteristics. There were no significant differences between the groups except in the prevalence of atrial fibrillation. There was no significant difference in oxygen flow rate between the groups (conventional therapy group: 9.2 ± 3.7 L/min, ASV therapy group: 11.4 ± 1.2 L/min). Mean time of ASV use and following mean oxygen flow rate after ASV therapy were 9.8 ± 5.8 h and 2.2 ± 1.5 L/min. Fig. 3

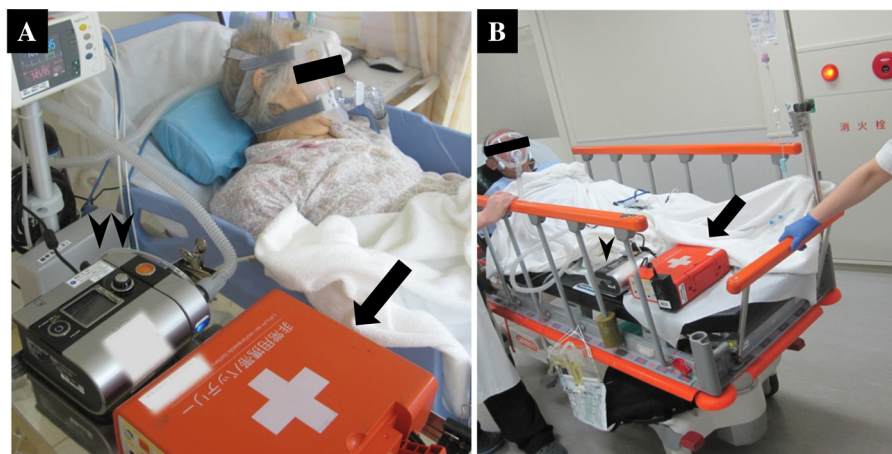


Fig. 1. The initial settings for adaptive servo-ventilation. Adaptive servo-ventilation (arrowhead) combined with a small battery (arrow) applied in the emergency room (A), and during transportation (B).

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