Successful termination of recurrent ventricular arrhythmias by adaptive servo-ventilation in a patient with heart failure

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Summary
A 60-year-old woman who underwent operation due to severe aortic stenosis with left ventricular dysfunction had frequent nonsustained ventricular tachycardia (NSVT) at night. She had an increased apnea–hypopnea index and a reduction in minimum O2 saturation during sleep, which was closely associated with the frequency of NSVT. Adaptive servo-ventilation (ASV) therapy improved sleep disorder breathing (SDB) and also reduced ventricular arrhythmias. These effects were associated with the attenuation of the sympathetic nerve activities by the analysis of heart rate variability. ASV is expected to be effective in the treatment of ventricular tachyarrhythmias in patients with heart failure and SDB.

Introduction
Patients with heart failure (HF) often have sleep disorder breathing (SDB), especially Cheyne–Stokes respiration. The prevalence of this association has been reported to be between 40% and 50% in HF [1,2]. SDB has been shown to be associated with an increased risk for the fatal arrhythmias and sudden cardiac death [3]. Approximately 20–35% of patients with SDB have premature ventricular contraction and 3.0–5.3% of those have nonsustained ventricular tachycardia (NSVT) [4,5], suggesting that SDB may trigger lethal ventricular arrhythmias. In patients with SDB, recurrent nocturnal apnea and hypopnea during sleep activate sympathetic nerve activity, which may not only worsen HF but also trigger lethal ventricular arrhythmias. Adaptive servo-ventilation (ASV) is a novel therapy for SDB in patients with HF [6]. It can not only normalize the pattern of respiration and quality of sleep, but also stabilize sympathetic nerve activity [7]. Therefore, it is also expected to reduce lethal arrhythmias in patients with HF and SDB. This is a...
Figure 1 The electrocardiogram monitor shows sustained ventricular tachycardia terminated by the anti-tachycardia pacing of the implantable cardioverter-defibrillator.

first report showing successful termination of ventricular arrhythmias including NSVT by ASV in a patient with chronic HF.

Case report

A 60-year-old woman who had undergone aortic valve replacement for severe aortic stenosis with left ventricular (LV) dysfunction and prior history of pulmonary edema was admitted to our cardiology ward for the treatment of HF. On admission, her heart rate was 60 beats per minute, and blood pressure was 94/68 mmHg. She did not have jugular venous distension, lower leg edema, or rales. A 12-lead electrocardiogram (ECG) revealed complete atrioventricular block with junctional escape rhythm and sporadic episodes of NSVT. Chest X-ray showed slight enlargement of the heart, cardiothoracic ratio 56%, but no obvious pulmonary congestion. Serum creatinine was 1.0 mg/dl, and plasma brain natriuretic peptide (BNP) value was elevated to 659 pg/ml. Echocardiography showed diffuse LV hypokinesia with ejection fraction (EF) of 27%. No abnormalities in prosthetic aortic valve were detected. The septal to posterior wall motion delay was 264 ms, and tissue Doppler echocardiography demonstrated that the standard deviation of time to peak systolic velocity of 12 segments of the LV wall at the basal and medial levels was 41.3 ms, indicating the presence of LV dyssynchrony. She had standard medical treatment including carvedilol 10 mg, enalapril 2.5 mg, furosemide 60 mg, spironolactone 50 mg, and amiodarone 400 mg. Cardiac resynchronization therapy with defibrillator was performed for the treatment of HF with low EF and complete atrioventricular block. Even after the stabilization of HF, frequent NSVT persisted and electrical storm terminated by implantable cardioverter-defibrillator occurred mainly during sleep (Figs. 1–3). A portable sleep monitoring device type 3 (Morpheus; Teijin Pharma, Tokyo, Japan) [8] revealed that apnea—hypopnea index (AHI) was 15.2/h and minimum oxygen saturation (SpO₂) was decreased to 84% at night, confirming the presence of SDB, mainly obstructive sleep apnea (Fig. 3). Moreover, 24-h ECG monitoring showed that ventricular arrhythmias such as premature ventricular contraction (PVC) and NSVT were noted during sleep (Fig. 2), which coincided with the decrease in SpO₂. ASV (Auto Set CS; Teijin Pharma, Tokyo) was started without oxygenation and full face masks (Teijin Pharma) in the default settings; expiratory positive airway pressure of 5 cm H₂O, inspiratory...
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As expected, AHI decreased to 5.5/h and minimum SpO2 increased to 91% after ASV (Fig. 2 and Table 1). In parallel to this improvement in SDB, the number of NSVT and sustained VT remarkably decreased from 25.3 to 1.4/h (Fig. 2 and Table 1). Moreover, PVC count and NSVT were dramatically decreased from 297.8 to 67.3/h (Fig. 3 and Table 1). Furthermore, these beneficial effects of ASV on SDB and ventricular arrhythmias were associated with the attenuation of activated sympathetic nervous activity at night as assessed by low frequency domain/high frequency domain (LF/HF) by the analysis of heart rate variability (Fig. 3 and Table 1).

### Discussion

This report demonstrated that ASV therapy was effective for ventricular arrhythmias including NSVT in a HF patient with SDB. PVC and NSVT are commonly associated with SDB [4,5]. Moreover, the frequency of PVCs has been shown to be positively correlated with severity of SDB in HF patients [1]. Previous studies reported that continuous positive airways pressure (CPAP) therapy was effective in reducing arrhythmias in patients with SDB. In obstructive sleep apnea patients with HF, CPAP therapy improved LVEF, and reduced the frequency of PVC during sleep by 58% [9]. Shimada et al. [10] also reported CPAP could reduce the incidence of NSVT in HF patients with SDB. In contrast, Craig et al.
Figure 4  AHI (A) and minimum SpO2 (B) before and during ASV. ASV, adaptive servo-ventilation; AHI, apnea hypopnea index; SpO2, oxygen saturation.

[11] could not demonstrate a decrease in arrhythmia frequency in patients with SDB. ASV is one of the new therapies for HF patients with SDB. Oldenburg et al. [6] reported that ASV could improve SDB, exercise capacity, LVEF, and N-terminal pro BNP in patients with HF and central sleep apnea. However, the effects of ASV on ventricular arrhythmias have never been demonstrated in previous reports. Therefore, the present findings that ASV therapy was effective for arrhythmias are the first report, which may uncover its efficacy in the treatment of HF. They are the extension of the previous findings obtained by CPAP [10]. However, we consider that ASV can be superior to CPAP for the suppression of serious ventricular arrhythmias because ASV is expected to effectively inhibit sympathetic nervous system activities compared with CPAP. There are several postulated mechanisms that sympathetic nervous system activated by SDB can result in fatal arrhythmias. At first, hypoxia and hypercapnia induced by SDB activate the sympathetic nervous system via the chemoreceptors of the carotid artery, aortic arch or respiratory control center, which cause frequent PVCs and fatal arrhythmias [12,13]. Secondly, the suppression of the extension of lungs by the apnea inhibits the activity of the vagal nerve and inversely activates the sympathetic nerve [14]. Finally, sleep fragmentation due to the apnea also causes sympathetic hyperactivity [15]. ASV can support the breathing of the pressure wave form similar to spontaneous respiration and maintain 90% of the average minute ventilation during most recent 3 min by regulating IPAP and timing of the backup support automatically based on the default mechanical setting, which may minimize the activation of sympathetic activity [16]. In fact, the present study demonstrated that the activated sympathetic nervous activity was attenuated after ASV assessed by LH/HF (Fig. 2). These findings are also supported by the report by Gür et al. [7] that ASV could decrease serum levels of epinephrine and norepinephrine.

ASV is one of the most effective devices for the appropriate regulation of sympathetic nerve in noninvasive intermittent positive pressure ventilation. It may be worth using ASV in order to control fatal arrhythmias in addition to the administration of antiarrhythmic drugs. The present report suggests that ASV can improve the long-term prognosis for patients with chronic HF by reducing cardiac events including sudden death or fatal arrhythmias, which, however, needs to be evaluated by a randomized controlled trial.

There are several limitations in this report. First we could not compare the effects of ASV on arrhythmias with other noninvasive methods of ventilation. Second, accurate polysomnography with electroencephalogram was not performed. Therefore we could not evaluate the exact correlation between sleep, breathing, and the sympathetic nerve. Finally, we had no data of sympathetic nervous activity in day-time by using ambulatory electrocardiographic
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In conclusion, ASV could be effective for the termination of recurrent NSVT in patients with HF and SDB.

References


