end-expiratory pulmonary volume and alveolar pressure, (3) assist inspiratory muscles,[4] (4) decrease left ventricular volume leading to the improvement in mitral regurgitation,[16, 29] (5) attenuate sympathetic nervous activity resulting in the suppression of lethal arrhythmias,[30-32] and (6) anti-inflammatory effect.[19] In the present study, we showed that ASV improved apnea indices and reduced left ventricular volume along with the decrease of functional MR. It has been suggested that ASV improved cardiac function and event-free survival of patients with HF and CSR-CSA with these mechanisms. Studies for effects of ASV on sympathetic nervous activity and inflammation are under investigation in our laboratory.

Study limitations

First, this was not a randomized study. Since we cannot randomize the study subjects, patients who were cooperative with ASV treatment were assigned to the ASV group. As a result, ASV group included more severe CSR-CSA than Non-ASV group. Second, the sample size was small, since this study was performed in a single institution. Further randomized study with a larger population is needed to establish ASV as a promising therapy for HF.

Conclusions

In this study, improvement in Cheyne-Stokes respiration was confirmed by titration of adaptive servo ventilation. To the best of our knowledge, the present study is the first to show the beneficial effects of adaptive servo ventilation on cardiac functional parameters, plasma BNP levels, and importantly reduced mortality and

re-hospitalization rates. These results suggest that adaptive servo ventilation might be a promising useful tool for heart failure as an important non-pharmacotherapy.

REFERENCES

1. Sin DD, Fitzgerald F, Parker JD, Newton G, Floras JS, Bradley TD. Risk factors for central and obstructive sleep apnea in 450 men and women with congestive heart failure. Am J Respir Crit Care Med 1999;160:1101-6.

2. Wang H, Parker JD, Newton GE, Floras JS, Mak S, Chiu KL, et al. Influence of obstructive sleep apnea on mortality in patients with heart failure. J Am Coll Cardiol 2007;49:1625-31.

3. Javaheri S, Shukla R, Zeigler H, Wexler L. Central sleep apnea, right ventricular dysfunction, and low diastolic blood pressure are predictors of mortality in systolic heart failure. J Am Coll Cardiol 2007;49:2028-34.

4. Oldenburg O, Schmidt A, Lamp B, Bitter T, Muntean BG, Langer C, et al. Adaptive servo ventilation improves cardiac function in patients with chronic heart failure and Cheyne-Stokes respiration. Eur J Heart Fail 2008;10:581-6.

5. Shiomi T, Guilleminault C, Stoohs R, Schnittger I. Leftward shift of the interventricular septum and pulsus paradoxus in obstructive sleep apnea syndrome. Chest 1991;100:894-902.

6. Buda AJ, Pinsky MR, Ingels NB, Jr., Daughters GT, 2nd, Stinson EB, Alderman EL. Effect of intrathoracic pressure on left ventricular performance. N Engl J Med 1979;301:453-9.

7. Teschler H, Dohring J, Wang YM, Berthon-Jones M. Adaptive pressure support servo-ventilation: a novel treatment for Cheyne-Stokes respiration in heart failure. Am J Respir Crit Care Med 2001;164:614-9.

8. Philippe C, Stoica-Herman M, Drouot X, Raffestin B, Escourrou P, Hittinger L, et al. Compliance with and effectiveness of adaptive servoventilation versus

continuous positive airway pressure in the treatment of Cheyne-Stokes respiration in heart failure over a six month period. Heart 2006;92:337-42.

9. Otsuka N, Ohi M, Chin K, Kita H, Noguchi T, Hata T, et al. Assessment of cardiac sympathetic function with iodine-123-MIBG imaging in obstructive sleep apnea syndrome. J Nucl Med 1997;38:567-72.

10. Kaneko Y, Floras JS, Usui K, Plante J, Tkacova R, Kubo T, et al. Cardiovascular effects of continuous positive airway pressure in patients with heart failure and obstructive sleep apnea. N Engl J Med 2003;348:1233-41.

11. Bradley TD, Logan AG, Kimoff RJ, Series F, Morrison D, Ferguson K, et al. Continuous positive airway pressure for central sleep apnea and heart failure. N Engl J Med 2005;353:2025-33.

12. Arzt M, Floras JS, Logan AG, Kimoff RJ, Series F, Morrison D, et al. Suppression of central sleep apnea by continuous positive airway pressure and transplant-free survival in heart failure: a post hoc analysis of the Canadian Continuous Positive Airway Pressure for Patients with Central Sleep Apnea and Heart Failure Trial (CANPAP). Circulation 2007;115:3173-80.

13. Kasai T, Usui Y, Yoshioka T, Yanagisawa N, Takata Y, Narui K, et al. Effect of flow-triggered adaptive servo-ventilation compared with continuous positive airway pressure in patients with chronic heart failure with coexisting obstructive sleep apnea and Cheyne-Stokes respiration. Circ Heart Fail 2010;3:140-8.

14. Hastings PC, Vazir A, Meadows GE, Dayer M, Poole-Wilson PA, McIntyre HF, et al. Adaptive servo-ventilation in heart failure patients with sleep apnea: a real world study. Int J Cardiol 2010;139:17-24.

15. Bitter T, Westerheide N, Faber L, Hering D, Prinz C, Langer C, et al. Adaptive servoventilation in diastolic heart failure and Cheyne-Stokes respiration. Eur Respir J 2009.

16. Kasai T, Narui K, Dohi T, Takaya H, Yanagisawa N, Dungan G, et al. First experience of using new adaptive servo-ventilation device for Cheyne-Stokes respiration with central sleep apnea among Japanese patients with congestive heart failure: report of 4 clinical cases. Circ J 2006;70:1148-54.

17. Sulg IA. Manual EEG analysis. Acta Neurol Scand 1969;45:431-58.

18. EEG arousals: scoring rules and examples: a preliminary report from the sleep disorders atlas task force of the American Sleep Disorders Association. Sleep 1992;15:173-84.

19. Koyama T, Watanabe H, Kobukai Y, Makabe S, Munehisa Y, Iino K, et al. Beneficial effects of adaptive servo ventilation in patients with chronic heart failure. Circ J 2010.

20. Tamura A, Kawano Y, Kadota J. Carvedilol reduces the severity of central sleep apnea in chronic heart failure. Circ J 2009;73:295-8.

21. Tamura A, Kawano Y, Naono S, Kotoku M, Kadota J. Relationship between beta-blocker treatment and the severity of central sleep apnea in chronic heart failure. Chest 2007;131:130-5.

22. Sinha AM, Skobel EC, Breithardt OA, Norra C, Markus KU, Breuer C, et al. Cardiac resynchronization therapy improves central sleep apnea and Cheyne-Stokes respiration in patients with chronic heart failure. J Am Coll Cardiol 2004;44:68-71.

23. Oldenburg O, Faber L, Vogt J, Dorszewski A, Szabados F, Horstkotte D, et al. Influence of cardiac resynchronisation therapy on different types of sleep disordered breathing. Eur J Heart Fail 2007;9:820-6.

24. Walsh JT, Andrews R, Starling R, Cowley AJ, Johnston ID, Kinnear WJ. Effects of captopril and oxygen on sleep apnoea in patients with mild to moderate congestive cardiac failure. Br Heart J 1995;73:237-41.

25. Solin P, Bergin P, Richardson M, Kaye DM, Walters EH, Naughton MT. Influence of pulmonary capillary wedge pressure on central apnea in heart failure. Circulation 1999;99:1574-9.

26. Naughton MT, Liu PP, Bernard DC, Goldstein RS, Bradley TD. Treatment of congestive heart failure and Cheyne-Stokes respiration during sleep by continuous positive airway pressure. Am J Respir Crit Care Med 1995;151:92-7.

27. Pepperell JC, Maskell NA, Jones DR, Langford-Wiley BA, Crosthwaite N, Stradling JR, et al. A randomized controlled trial of adaptive ventilation for Cheyne-Stokes breathing in heart failure. Am J Respir Crit Care Med 2003;168:1109-14.

28. Sin DD, Logan AG, Fitzgerald FS, Liu PP, Bradley TD. Effects of continuous positive airway pressure on cardiovascular outcomes in heart failure patients with and without Cheyne-Stokes respiration. Circulation 2000;102:61-6.

29. Lanfranchi PA, Braghiroli A, Bosimini E, Mazzuero G, Colombo R, Donner CF, et al. Prognostic value of nocturnal Cheyne-Stokes respiration in chronic heart failure. Circulation 1999;99:1435-40.

30. Naughton MT, Benard DC, Liu PP, Rutherford R, Rankin F, Bradley TD. Effects of nasal CPAP on sympathetic activity in patients with heart failure and central sleep apnea. Am J Respir Crit Care Med 1995;152:473-9.

31. Mortara A, Sleight P, Pinna GD, Maestri R, Capomolla S, Febo O, et al. Association between hemodynamic impairment and Cheyne-Stokes respiration and periodic breathing in chronic stable congestive heart failure secondary to ischemic or idiopathic dilated cardiomyopathy. Am J Cardiol 1999;84:900-4.

32. Lanfranchi PA, Somers VK, Braghiroli A, Corra U, Eleuteri E, Giannuzzi P. Central sleep apnea in left ventricular dysfunction: prevalence and implications for arrhythmic risk. Circulation 2003;107:727-32.

FIGURE LEGENDS

Figure 1. Study design and populations.

Figure 2. Kaplan-Meier analysis for all cardiac events between patients with ASV and Non-ASV groups.

Table 1. Comparison of clinical characteristics between patients with ASV and Non-ASV groups.

		ASV (n=23)	Non-ASV (n=37)	P value
Physical	Age (years)	60.8 ± 13.7	60.5 ± 16.7	N.S
	Male (n,%)	20 (87.0)	29 (78.4)	N.S
	BMI	26.1 ± 4.4	24.1 ± 5.0	N.S
	NYHA (I/IIs/IIm/III/IV)	0/3/9/10/1	0/7/13/15/2	N.S
Etiology	Cardiomyopathy (n,%)	16 (69.5)	26 (70.3)	N.S
	Ischemic (n,%)	4 (17.4)	6 (16.2)	N.S
	Valvular (n,%)	3 (13.1)	5 (13.5)	N.S
Rhythm	Sinus rhythm (n,%)	8 (34.8)	14 (37.8)	N.S
	Atrial fibrillation (n,%)	8 (34.8)	12 (32.4)	N.S
	Pacemaker (n,%)	2 (8.7)	4 (10.8)	N.S
	CRT (n,%)	5 (21.7)	7 (18.9)	N.S
Medication	ACE inhibitors (n,%)	14 (60.9)	22 (59.5)	N.S
	ARBs (n,%)	9 (39.1)	11 (29.7)	N.S
	β blockers (n,%)	20 (87.0)	31 (83.8)	N.S
	Diuretics (n,%)	16 (69.6)	26 (70.3)	N.S
	Aldosterone antagonist (n,%)	14 (60.9)	23 (62.2)	N.S
	Digitalis (n,%)	3 (13.0)	2 (5.4)	N.S
	Amiodarone (n,%)	7 (30.4)	9 (24.3)	N.S
	Pimopendan (n,%)	4 (17.4)	6 (16.2)	N.S
Labo data	BNP (pg/ml)	499.0 ± 580.2	502.3 ± 409.4	N.S
	PaO_2 (mmHg)	96.5 ± 17.1	89.0 ± 22.3	N.S
	$PaCO_2$ (mmHg)	35.1 ± 4.6	36.8 ± 3.9	N.S
	Hb (g/dl)	13.1 ± 2.0	12.9 ± 2.3	N.S
	eGFR (ml/min/1.73cm^2)	63.4 ± 18.7	58.1 ± 24.5	N.S

NYHA, New York Heart Association; BMI, body mass index; CRT, cardiac resynchronization therapy; ACE, angiotensin-converting enzyme; ARB, angiotensin II receptor blocker; BNP, B-type natriuretic pepide; eGFR, estimated glomerrular filtration rate.

Table 2. Baseline data of echocardiography, spirogram and cardiothoracic ratio.

	ASV	Non-ASV	P value
LVEDVI (ml/m^2)	84.7 ± 39.0	81.2 ± 26.0	N.S
LVESVI (ml/m^2)	56.3 ± 36.2	50.8 ± 23.1	N.S
LVEF (%)	38.3 ± 18.4	38.9 ± 12.9	N.S
LVMI (g/m^2)	171.5 ± 70.7	152.4 ± 46.4	N.S
LAVI (ml/m^2)	52.3 ± 21.2	46.3 ± 5.1	N.S
RVPS (mmHg)	39.4 ± 20.5	39.4 ± 17.7	N.S
E/e'	13.2 ± 6.5	12.7 ± 7.8	N.S
%VC	93.8 ± 16.9	88.7 ± 19.3	N.S
FEV 1.0 (%)	79.5 ± 8.8	80.2 ± 11.7	N.S
CTR (%)	56.2 ± 6.4	57.0 ± 7.1	N.S

LVEDVI, left ventricular end diastolic volume index; LVESVI, left ventricular end systolic volume index; LVEF, left ventricular ejection fraction; LVMI, left ventricular mass index; LAVI, left atrial volume index; RVPS, right ventricular systolic pressure; %VC, % of vital capacity; FEV 1.0,% of forced expiratory volume in one second; CTR, cardio thoracic ratio.

Table 3. Baseline polysomnographic data

	ASV	Non-ASV	P value
AHI (times/h)	41.5 ± 15.8	33.1 ± 17.9	P<0.05
CAI (times/h)	21.4 ± 14.4	16.7 ± 12.9	N.S
CAI/AHI (%)	51.6	50.5	
OAI (times/h)	1.5 ± 2.5	6.0 ± 7.1	P<0.05
Arousal index	24.5 ± 8.2	23.7 ± 13.1	N.S
3% ODI (times/h)	33.3 ± 15.3	20.6 ± 16.7	P<0.01
Lowest SPO_2 (%)	76.0 ± 8.9	82.6 ± 9.3	P<0.01
Mean SPO_2 (%)	94.0 ± 3.0	95.7 ± 2.2	P<0.05
CT90 (%)	14.8 ± 19.0	8.8 ± 14.3	N.S
CT95 (%)	41.7 ± 30.9	31.6 ± 30.7	N.S
SWS (%)	2.1 ± 3.7	4.4 ± 7.5	N.S
REM sleep (%)	19.1 ± 6.4	16.3 ± 8.2	N.S
Sleep efficacy (%)	69.3 ± 14.0	63.4 ± 12.9	N.S

AHI, apnea hypopnea index; CAI, central apnea index; OAI, obstructive apnea index; ODI, oxidative desaturation index; Lowest SpO_2, lowest oxyhemoglobin saturation ; Mean SpO_2 , mean oxyhemoglobin saturation; CT90, %time< SpO_2 90%/total sleep time ; CT95, %time< SpO_2 95%/total sleep time; SWS, slow wave sleep; REM, rapid eye movement.

Table 4. Setting and compliance data of ASV

Device setting	Mean	Range
EPAP (mmHg)	6.0 ± 2.0	4-10
IPAP min (mmHg)	6.6 ± 2.4	4-12
IPAP max (mmHg)	12.5 ± 4.1	8-20
PS min (mmHg)	0.5 ± 1.3	0-4
RR	Auto	Auto
Downloaded data		
%usage (%)	79.7 ± 30.3	12-100
Mean usage time (min)	377.6 ± 166.7	297-546
4h > usage (%)	53.6 ± 32.3	7.7-96.0

EPAP, expiratory positive airway pressure; IPAP, inspiratory positive airway pressure; PS, pressure support; RR, respiratory rate; %Usage, a ratio of the use days; 4h > usage (%), a ratio of the use days more than four hours.

Table 5. Results of polysomnographic findings at baseline and on ASV.

	Baseline	On ASV	P value
AHI (times/h)	38.8 ± 17.3	9.0 ± 7.9	P<0.01
CAI (times/h)	19.5 ± 14.0	1.6 ± 2.1	P<0.01
CAI/AHI (%)	50.3	17.8	
OAI (times/h)	2.3 ± 3.7	1.0 ± 2.1	N.S
Arousal index	24.5 ± 9.7	15.9 ± 8.1	P<0.01
3%ODI (times/h)	30.1 ± 15.5	5.3 ± 7.3	P<0.01
Lowest SpO_2 (%)	77.4 ± 8.8	87.5 ± 7.8	P<0.01
Mean SpO_2 (%)	94.3 ± 2.8	96.6 ± 1.7	P<0.01
CT90 (%)	11.9 ± 17.3	1.1 ± 2.9	P<0.01
CT95 (%)	38.0 ± 30.7	11.8 ± 24.2	P<0.01
SWS (%)	2.5 ± 4.9	4.8 ± 8.7	P<0.05
REM Sleep (%)	18.2 ± 7.4	16.0 ± 5.2	N.S
Sleep Efficacy (%)	66.7 ± 14.0	72.3 ± 14.2	P<0.05

Abbreviations as in Table 3.

Table 6. Time course of NYHA functional class, BNP, and $PaCO_2$

	Baseline	3 mo	6 mo	Pvalue
NYHA functional class				
ASV	2.5 ± 0.6	-	1.6 ± 0.5	P<0.05
Non-ASV	2.6 ± 0.6	-	2.2 ± 0.7	N.S
BNP (pg/ml)				
ASV	499.0 ± 580.2	257.9 ± 249.8	191.6 ± 218.8	P<0.01
Non-ASV	502.3 ± 409.4	453.6 ± 465.5	475.2 ± 585.9	N.S
$PaCO_2$ (mmHg)				
ASV	35.3 ± 4.8	-	39.8 ± 4.5	P<0.05
Non-ASV	36.9 ± 3.9	-	38.4 ± 4.8	N.S

P<0.05 vs. Baseline

NYHA, New York Heart Association; BNP, B-type natriuretic pepide.

Table 7. Time course of cardiac function by determined by echocardiography

	Baseline	3 mo	6 mo	P value
LVEDVI (ml/m^2)				
ASV	84.7 ± 39.0	84.4 ± 39.4	75.7 ± 34.8	P<0.05
Non-ASV	81.2 ± 26.0	83.4 ± 38.1	81.8 ± 33.2	N.S
LVESVI (ml/m^2)				
ASV	56.3 ± 36.2	51.5 ± 34.2	42.2 ± 26.8	P<0.05
Non-ASV	50.8 ± 23.1	54.1 ± 34.6	50.5 ± 29.4	N.S
LVEF (%)				
ASV	38.3 ± 18.4	42.6 ± 15.8	46.4 ± 15.4	P<0.05
Non-ASV	38.9 ± 12.9	37.9 ± 14.0	41.2 ± 14.7	N.S
LVMI (g/m^2)				
ASV	171.5 ± 70.7	163.5 ± 47.7	153.5 ± 42.9	P<0.05
Non-ASV	152.4 ± 46.4	152.7 ± 46.0	148.6 ± 43.2	N.S
LAVI (ml/m^2)				
ASV	52.3 ± 21.2	49.3 ± 24.6	46.0 ± 20.0	P<0.05
Non-ASV	46.3 ± 25.1	49.3 ± 26.7	49.2 ± 27.0	N.S
RVPS (mmHg)				
ASV	39.4 ± 20.5	34.7 ± 13.0	32.9 ± 17.4	P<0.05
Non-ASV	39.4 ± 17.7	38.2 ± 14.5	38.8 ± 15.3	N.S
E/e'				
ASV	13.2 ± 6.5	11.4 ± 5.1	9.0 ± 4.7	P<0.05
Non-ASV	12.7 ± 7.8	13.6 ± 7.6	14.0 ± 7.6	N.S
MR score				
ASV	2.1 ± 0.3	1.7 ± 0.3	1.7 ± 0.2	P<0.05
Non-ASV	2.1 ± 0.2	2.1 ± 0.2	1.9 ± 0.2	N.S

Abbreviations as in Table 2.

Figure 1

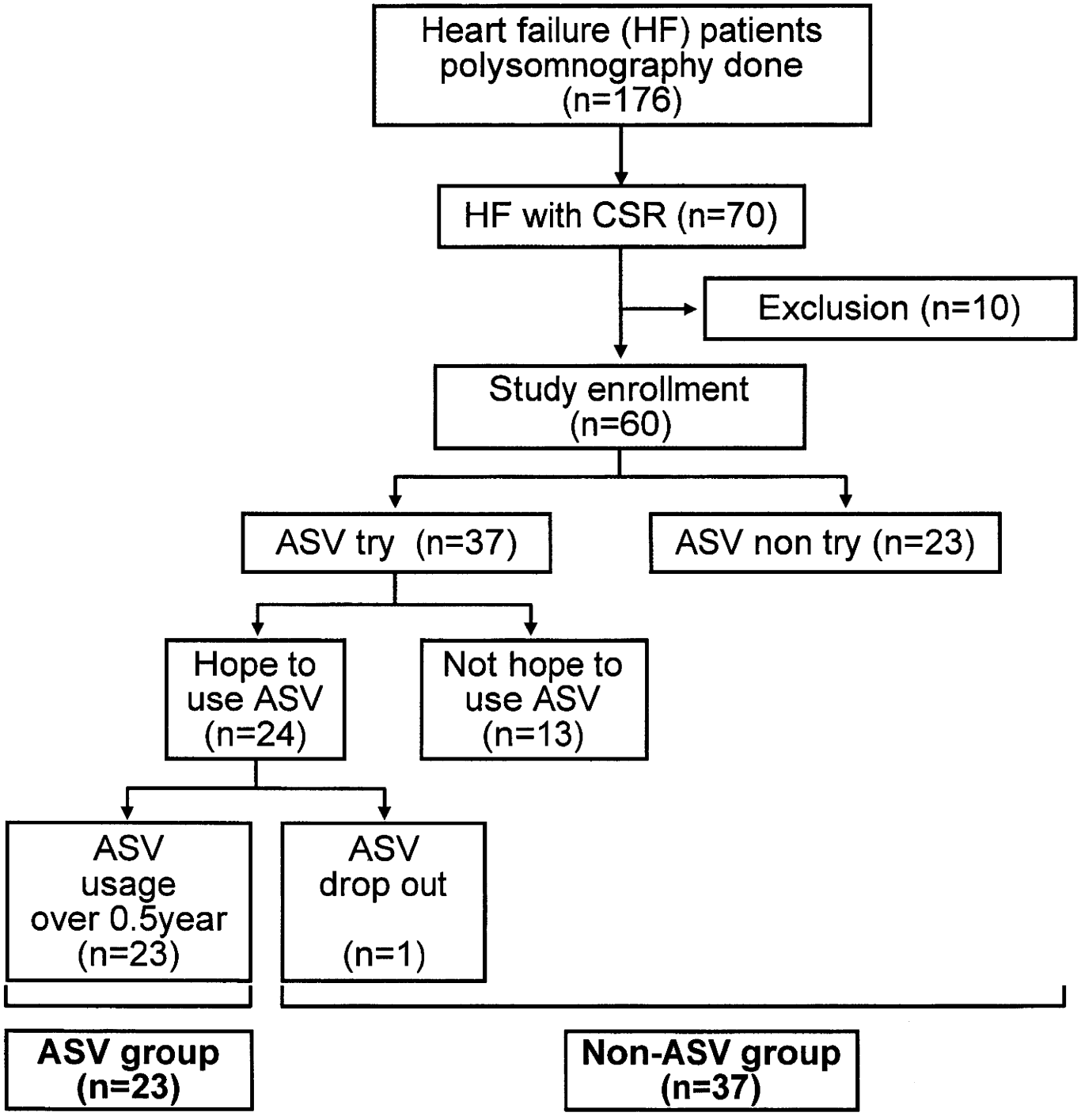
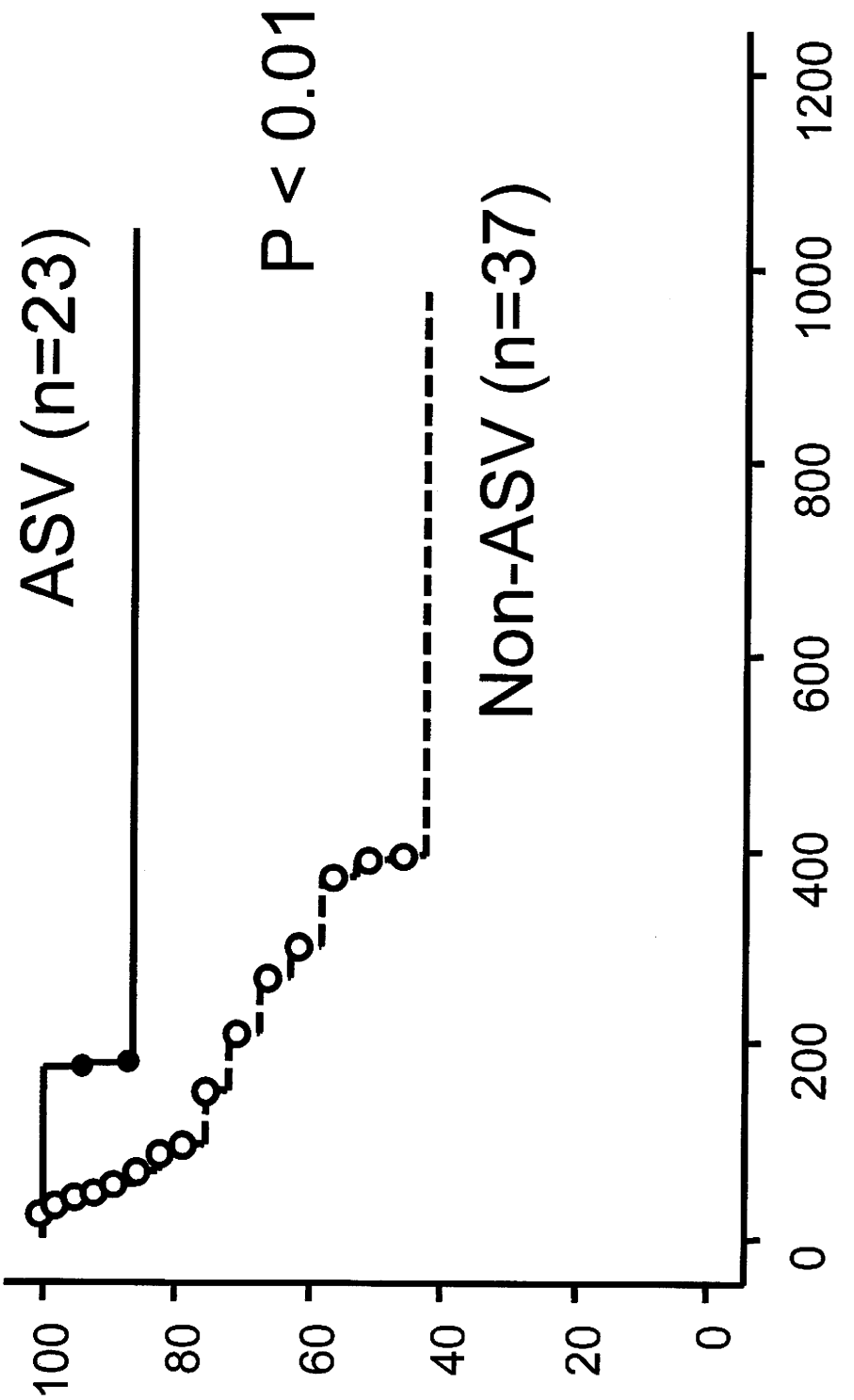

Heart failure (HF) patients polysomnography done (n=176)
HF with CSR (n=70)
Exclusion (n=10)
Study enrollment (n=60)
ASV try (n=37)
ASV non try (n=23)
Hope to use ASV (n=24)
Not hope to use ASV (n=13)
ASV usage over 0.5year (n=23)
ASV drop out (n=1)
ASV group (n=23)
Non-ASV group (n=37)

Figure 2


ASV (n=23)
P < 0.01
Non-ASV (n=37)
100
80
60
40
20
0
0
200
400
600
800
1000
1200

Acute decompensated heart failure syndromes (ATTEND) registry. A prospective observational multicenter cohort study: Rationale, design, and preliminary data

Naoki Sato, MD,[a] Katsuya Kajimoto, MD,[b] Kuniya Asai, MD,[c] Masayuki Mizuno, MD,[d] Yuichiro Minami, MD,[d] Michitaka Nagashima, MD,[d] Koji Murai, MD,[a] Ryo Muanakata, MD,[a] Dai Yumino, MD,[d] Tomomi Meguro, MD,[e] Masatoshi Kawana, MD,[f] Jun Nejima, MD,[g] Toshihiko Satoh, MD,[h] Kyoichi Mizuno, MD,[c] Keiji Tanaka, MD,[a] Hiroshi Kasanuki, MD,[i] and Teruo Takano, MD[c] for the ATTEND Investigators[j] *Tokyo and Kanagawa, Japan*

Acute heart failure syndromes (AHFS) are likely to increase in the future, and the high readmission rate of patients with AHFS is an important issue in Western countries. However, there are very few published epidemiological studies on AHFS in the Asia Pacific region. Because AHFS are heterogeneous, the characteristics, clinical profile, and management of AHFS should be clarified in an epidemiological study. The acute decompensated heart failure syndromes (ATTEND) registry is a prospective, observational, multicenter cohort study being performed in Japan and is the first epidemiological study of AHFS in the Asia Pacific region. This study is designed to investigate several aspects of AHFS as follows: (1) the registry allows patient-based data collection for precise evaluation of patient characteristics and short-term outcomes, including the readmission rate; (2) confirmation of clinical assessments can be performed, and new clinical assessments can be created; and (3) feedback allows the modification of guidelines for clinical management. The present report describes the clinical characteristics of patients with AHFS in Japan based on the preliminary data collected in this study, and the similarities and differences in characteristics of these patients compared with those in Western countries. Although most of the patient characteristics did not differ from those reported in Western studies, there are some unique findings in this study, including a high rate of treatment with carperitide (69.4%) and angiotensin II receptor blockers (53.9%) at discharge and a longer hospital stay (median 21 days). The ATTEND registry is designed to provide valuable information to clarify the characteristics of patients with AHFS to improve their management. (Am Heart J 2010;159:949-955.e1.)

The prevalence of acute heart failure syndromes (AHFS) is expected to increase in the future, despite improved rates of in-hospital mortality. The readmission rate is a high 50% at 6 months,[1] which resulted in an estimated cost of >$37 billion for heart failure care in the United States during 2009,[2] suggesting that the increasing prevalence and high readmission rate of AHFS are critical issues for developed countries. Therefore, patient-based, rather than event-based, data for AHFS are essential to reduce the number of hospital admissions by verifying the extent of compliance with heart failure management guidelines and to improve clinical assessment and prognostic tools.

In the Asia Pacific region, published information on the epidemiology and clinical management of AHFS is virtually nonexistent.[3] This lack of information is a major barrier to the attempts and global collaboration and discussion of relevant issues. It is important to perform international comparisons and identify any differences to provide information about whether the clinical guidelines and evidence obtained from Western countries can be applied to patients with AHFS in the Asia Pacific region.

Therefore, the main goals of the present study were to clarify the overall clinical characteristics of patients

From the [a]Intensive and Cardiac Care Unit, Nippon Medical School, Tokyo, Japan, [b]Department of Cardiology, Sensoji Hospital, Tokyo, Japan, [c]Department of Internal Medicine, Nippon Medical School, Tokyo, Japan, [d]Department of Cardiology, Tokyo Women's Medical University, Tokyo, Japan, [e]Department of Internal Medicine, Tokyo Denryoku Hospital, Tokyo, Japan, [f]Department of Cardiology, Tokyo Women's Medical University, Aoyama Hospital, Tokyo, Japan, [g]Department of Internal Medicine, Tsurumi University School of Dental Medicine, Kanagawa, Japan, [h]Kitasato Clinical Research Center, Kitasato University School of Medicine, Kanagawa, Japan, and [i]Faculty of Science and Engineering, Waseda University, Tokyo, Japan.

[j]See Appendix online for complete listing of the ATTEND Investigators.

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Reprint requests: Naoki Sato, MD, Intensive and Cardiac Care Unit, Nippon Medical School, 1-1-5 Sendagi, Bunkyo-ku, Tokyo 113-8603, Japan.

E-mail: nms-ns@nms.ac.jp

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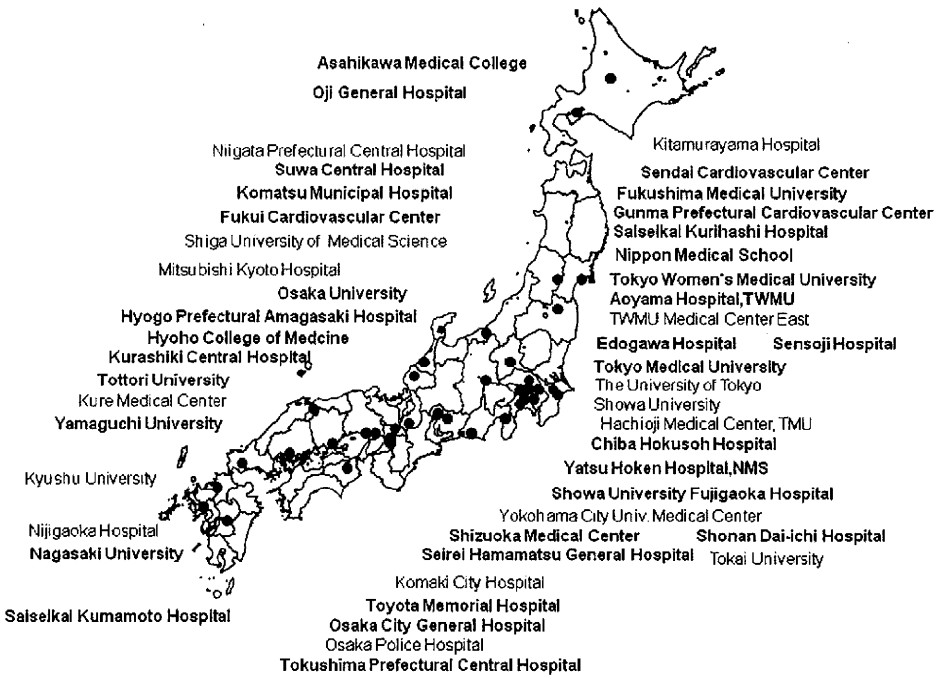
Figure 1



Forty-seven hospitals have been selected and 32 hospitals (indicated in bold letters) were enrolling patients as of June 16, 2009. The ATTEND registry is still recruiting hospitals and participants.

with AHFS in Japan and the similarities and differences in patient characteristics and management of AHFS in Japan compared with those in Western countries.

Methods

Study design

The acute decompensated heart failure syndromes (ATTEND) registry is a prospective observational multicenter cohort study that is currently underway in Japan. Patients are enrolled at the first admission and then followed up; thus, data collection is patient based and not event based.

Study objectives

The objectives of the ATTEND registry are to clarify the overall clinical characteristics of patients with AHFS, including (1) demographic characteristics and clinical profile, (2) current treatments, (3) short-term outcomes, and (4) comparison with representative epidemiological data in Western countries including ADHERE,[1-6] OPTIMIZE-HF,[7,8] and EHFS II.[9]

Information disclosure

Before the launch of the ATTEND registry, information on the objectives of the present study, its social significance, and an abstract were provided for clinical trial registration with the University Hospital Medical Information Network (UMIN 000000736), which is recognized by the International Committee of Medical Journal Editors as an "acceptable registry" according to a statement issued in September 2004.[10]

Participants

In-patients with AHFS who met the modified Framingham criteria, which only includes variables estimated at admission in Framingham criteria,[11] are eligible for the study. Patients aged <20 years and patients who are not considered suitable by the attending physicians are excluded. The present study rules out acute coronary syndromes (ACS). The ATTEND registry started enrolling patients in April 2007 and is expected to be completed by September 30, 2012, with a planned follow-up of 180 days for each patient.

The participating hospitals included academic and nonacademic hospitals and cardiac care units that were selected with consideration of their geographical distribution (Figure 1). The study protocol was approved by the ethics committee at each site. Forty-seven hospitals were selected, of which 32 hospitals are currently enrolling patients and the others are preparing for enrollment (as of June 16, 2009). The enrollment starting dates vary between participating hospitals because enrollment could only start at each hospital after approval by the relevant ethics committee. Therefore, to date, the number of patients enrolled is unevenly distributed between the participating hospitals.

Procedures and data collection

Written informed consent must generally be obtained from each patient. Because in-patients with AHFS may not be able to

Table I. Clinical characteristic of patients hospitalized with AHFS: A comparison of 4 epidemiological studies

	ATTEND	ADHERE	OPTIMIZE-HF	EHFS II
	n = 1110	n = 187,565	n = 48,612	n = 3580
Demographics				
Age, mean ± SD, y	73 ± 14	72 ± 14*	73 ± 14	70 ± 13
Men, %	59	49	48	61
Comorbidities, %				
Hypertension	71	74	71	63
Diabetes mellitus	34	44	42	33
Stroke/transient ischemic attack	12	17	16	13
Atrial fibrillation/flutter	40	31	31†	39
Chronic obstructive pulmonary disease	9	29	28	19
Etiology				
Ischemic, %	33	57	46	30‡
Hypertensive, %	18	N/A	23	11
Clinical status on admission				
De novo AHF	63	24	13§	37
Orthopnea	69	34‖	27	N/A
Peripheral edema	68	65	65	N/A
Creatinine level, mean ± SD, mg/dL	1.4 ± 1.5	1.8 ± 1.6¶	1.8 ± 1.8	N/A
Brain natriuretic peptide, mean ± SD or median, pg/mL	1063 ± 1158	Median 843	1273 ± 1330	N/A
Heart rate, mean ± SD or median, beat/min	99 ± 30	N/A	87 ± 22	Median 95
SBP, mean ± SD, mm Hg	147 ± 38	144 ± 33*	143 ± 33	N/A
Median, mm Hg	141	N/A	N/A	135
LVEF <40%	57	47	48.8	46
Outcomes				
Length of stay, median, d	21	4.3	N/A	9
Mean, d	31	N/A	6.4	N/A
In-hospital mortality, %	7.7	3.8	3.8	6.7

Values are shown as percentage, mean ± SD, or median. N/A indicates not available.
*n = 159,168 from Fonarow et al.[5]
†Atrial fibrillation.
‡Acute coronary syndromes.
§Data from Gheorghiade et al.[7]
‖Dyspnea at rest.
¶n = 105,388 from Adams et al.[6]

give consent due to their disease severity, informed consent can be obtained from a relative or legal representative in these circumstances. Consent is not required if patients die during hospitalization according to the Japanese ethical guidelines. Each patient's personal information is carefully managed based on the "Guidelines for the Adequate Management of Personal Information in Health/Nursing Field."

Once informed consent is obtained, the attending physicians fill out an ATTEND case report at discharge and sends it to the data center. After discharge, the attending physicians must update the status of events on the ATTEND Web database at appropriate times. Data on registered patients are collected from the ATTEND case report. Underlying diseases are diagnosed at discharge according to the American College of Cardiology/American Heart Association clinical data standards.[12]

At admission, the patient's history is obtained and included heart failure–related admissions, atrial flutter or fibrillation, ventricular tachycardia and fibrillation, continuous positive airway pressure, pacemaker, cardiac resynchronization therapy with or without defibrillation, implantable cardioverter-defibrillator, stroke/transient ischemic attack, dialysis, chronic respiratory disease, bronchial asthma, hypertension, dyslipidemia, diabetes, and smoking. Physical examination is performed at admission to assess the following: New York Heart Association functional class; noninvasive hemodynamic assessments by the absence or presence of congestion assessed by orthopnea, rales, elevation of jugular venous pressure, abdominal jugular reflux, hepatomegaly, ascites, and edema; and adequacy of perfusion assessed by low proportional pulse pressure (<25%), cold extremities, altered mentation, worsening renal function, paroxysmal nocturnal dyspnea, orthopnea, rales, third heart sound, jugular venous distention, edema, coldness of the extremities and also oxygen saturation by pulse oximetry, systolic and diastolic blood pressures, and heart rate. Based on these assessments, patients can be described as "warm and dry," "warm and wet," "cold and wet," or "cold and dry."[13] Echocardiography is also performed at admission and discharge, whereas the left atrial and ventricular dimensions are measured at discharge only. Biochemistry tests are done at admission and before discharge, including blood urea nitrogen, serum creatinine level, serum sodium, hemoglobin level, C-reactive protein, total bilirubin, brain natriuretic peptide, total cholesterol, triglycerides, and high-density lipoprotein cholesterol.

Treatment information, including the medications used before admission and at discharge and intravenous agents administered during the early phase of hospitalization, is obtained and entered into the case report. Short-term morbidity