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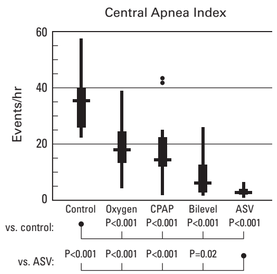
Adaptive pressure support servo-ventilation: a novel treatment for Cheyne-Stokes respiration in heart failure.

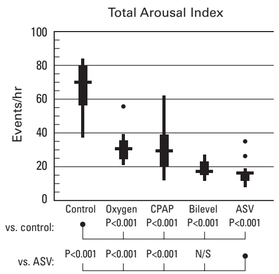
Teschler H, Dohring J, Wang YM, Berthon-Jones M.

Faculty of Medicine, Ruhrlandklinik, University of Essen, Essen, Germany. Helmutt@t-online.de

Adaptive servo-ventilation (ASV) is a novel method of ventilatory support designed for Cheyne-Stokes respiration (CSR) in heart failure. The aim of our study was to compare the effect of one night of ASV on sleep and breathing with the effect of other treatments. Fourteen subjects with stable cardiac failure and receiving optimal medical treatment were tested untreated and on four treatment nights in random order: nasal oxygen (2 L/min), continuous positive airway pressure (CPAP) (mean 9.25 cm H(2)O), bilevel (mean 13.5/5.2 cm H(2)O), or ASV largely at the default settings (mean pressure 7 to 9 cm H(2)O) during polysomnography. Thermistor apnea + hypopnea index (AHI) declined from 44.5 +/- 3.4/h (SEM) untreated to 28.2 +/- 3.4/h oxygen and 26.8 +/- 4.6/h CPAP (both $p < 0.001$ versus control), 14.8 +/- 2.3/h bilevel, and 6.3 +/- 0.9/h ASV ($p < 0.001$ versus bilevel). Effort band AHI behaved similarly. Arousal index decreased from 65.1 +/- 3.9/h untreated to 29.8 +/- 2.8/h oxygen and 29.9 +/- 3.2/h CPAP, to 16.0 +/- 1.3/h bilevel and 14.7 +/- 1.8/h ASV ($p < 0.01$ versus all except bilevel). There were large increases in slow-wave and rapid eye movement (REM) sleep with ASV but not with oxygen or CPAP. All subjects preferred ASV to CPAP. One night ASV suppresses central sleep apnea and/or CSR (CSA/CSR) in heart failure and improves sleep quality better than CPAP or 2 L/min oxygen.



Box plots of effect of treatment on central apnea index. *Horizontal bar:* median; *thick vertical line:* interquartile range; *circles:* outliers; *thin bar:* range excluding outliers. Also shown are statistical significance of comparisons between control and each of the four treatments, and between ASV and the other four conditions.



Box plots of effect of treatment on arousal index. Legend as for Figure 1.

Heart 2005 Jan 20

Compliance with and efficacy of adaptive servo-ventilation (ASV) versus continuous positive airway pressure (CPAP) in the treatment of Cheyne-Stokes respiration in heart failure over a six month period.

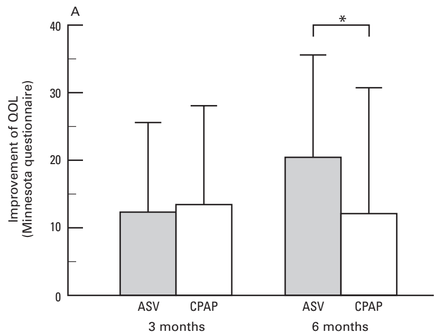
Philippe C, Stoica-Herman M, Drouot X, Raffestin B, Escourrou P, Hittinger L, Michel PL, Rouault S, d'Ortho MP.

Hopital Tenon, AP-HP, France.

Aim: Central sleep apnoea syndrome (CSA) with Cheyne-Stokes respiration (CSR) has an important influence on prognosis of congestive heart failure (CHF). Nocturnal Continuous Positive Airway Pressure (CPAP) has been found to improve transplant-free survival. Adaptive Servo-Ventilation (ASV) is a novel positive pressure mode that provides servo-controlled bi-level pressure support. The present study compared the compliance with and efficacy of ASV to CPAP, in patients with CSA-CSR and CHF, using Apnoea Hypopnoea Index (AHI), quality of life and LVEF over 6 months.

Methods and results: 25 patients (age: 28-80y, NYHA: II-IV) with stable CHF and CSA-CSR were randomised to either CPAP or ASV. At inclusion, both groups were comparable for NYHA class, LVEF, medical treatment, BMI and CSA-CSR. Both ASV and CPAP decreased the AHI, but noticeably, only ASV completely corrected the sleep apnoea syndrome (SAS), with AHI below 10/h. At 3 months, compliance was comparable between ASV and CPAP, however, at 6 months compliance with CPAP was significantly less than with ASV. At 6 months, the improvement in quality of life was higher with ASV and only ASV induced a significant increase in LVEF.

Conclusion: These results suggest that patients with CSA-CSR might receive greater benefit from treatment with ASV than with CPAP.



(A) Change in quality of life (QOL) measured by the Minnesota living with heart failure questionnaire. The improvement in QOL is expressed by the positive difference between the baseline score minus the score at the considered time point, either three or six months. Both ASV and CPAP induced a significant improvement in QOL at three months, but the improvement observed *after six months was significantly greater with ASV than with CPAP.* Data are mean (SD).
* Significant difference.

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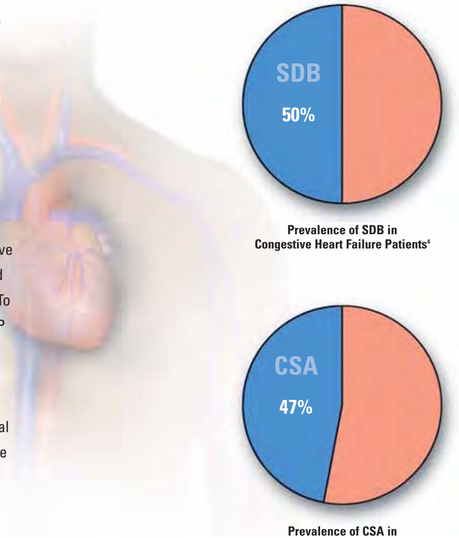
ResMed

Heart Failure and Central Sleep Apnea/ Cheyne-Stokes Respiration

Sleep-disordered breathing (SDB) is known to have serious cardiovascular consequences. Reseach indicates that up to 70% of patients with heart failure have some form of SDB[1] - either obstructive sleep apnea (OSA) or central sleep apnea (CSA)[2]. Furthermore, heart failure patients with CSA also often exhibit a form of periodic breathing, known as Cheyne-Stokes respiration (CSR), and these patients have been shown to have a very poor prognosis[3]. Currently available positive airway pressure (PAP) therapies have had mixed results for patients with CSA/CSR. To this end, ResMed has developed the VPAP Adapt SV™ to treat CSA/CSR in a home environment. This novel therapy utilises adaptive servo-ventilation (ASV) and has demonstrated the ability to improve clinical outcomes and quality of life in heart failure patients[4].



Prevalence of SDB in Congestive Heart Failure Patients[4]

Prevalence of CSA in Congestive Heart Failure patients with SDB[5]

1 Oldenburg et al, *Eur J Heart Fail Epub* Oct 5; 2006
2 Sin et al. *American Journal of Respiratory Critical Care Medicine*; 1999
3 Lafranchi et al. *Circulation*; 1999
4 Philippe et al. *Heart*; 2005
5 Javaheri et al. *Circulation*; 1998
6 Sin et al. *American Journal of Respiratory Critical Care Medicine*; 1999

Circulation 1999; 99(11):1435-1440

Prognostic value of nocturnal Cheyne-Stokes respiration in chronic heart failure.

Lanfranchi PA, Braghiroli A, Bosimini E, Mazzuero G, Colombo R, Conner CF, Giannuzzi P.

Division of Cardiology, Department of Bioengineering, Salvatore Maugeri Foundation, IRCCS, Veruno, Italy. planfranchi@fsm.it

Background: Nocturnal Cheyne-Stokes respiration (CSR) occurs frequently in patients with chronic heart failure (CHF), and it may be associated with sympathetic activation. The aim of the present study was to evaluate whether CSR could affect prognosis in patients with CHF.

Methods and results: Sixty-two CHF patients with left ventricular ejection fraction </=35%, in NYHA class II to III, underwent clinical evaluation, Doppler echocardiography, ergospirometry, phenylephrine test, Holter recording, and a sleep study to evaluate the occurrence of CSR, expressed as percentage of periodic breathing, and apnea/hypopnea index (AHI) (ie, the number of apneas and hypopneas per hour of recording). During a mean follow-up of 28+/-13 months, 15 patients died of cardiac causes. Nonsurvivors were in a higher NYHA functional class than survivors (P<0.001) and had a more depressed left ventricular ejection fraction (P<0.03), a shorter deceleration time of early filling (P<0.05), larger left and right atria (P<0.05 and P<0.02, respectively) and a lower peak $V(O_2)$ (P<0.05). Nonsurvivors also spent a greater percentage of the night in periodic breathing (P<0.01) with a greater AHI (P<0.03) and showed lower values of diurnal baroreflex sensitivity (P<0.05) and of heart rate variability (sdNN: P<0.01). Multivariate analysis revealed the AHI (chi2, 10.4; P<0.01), followed by left atrial area (chi2, 5.7; P<0.01), as the only independent and additional predictors of subsequent cardiac death. Patients at very high risk for fatal outcome could be identified by an AHI >/=30/h and left atria >/=25 cm_2.

Conclusions: The AHI is a powerful independent predictor of poor prognosis in clinically stable patients with CHF. The presence of an AHI >/=30/h adds prognostic information compared with other clinical, echocardiographic, and autonomic data and identifies patients at very high risk for subsequent cardiac death.

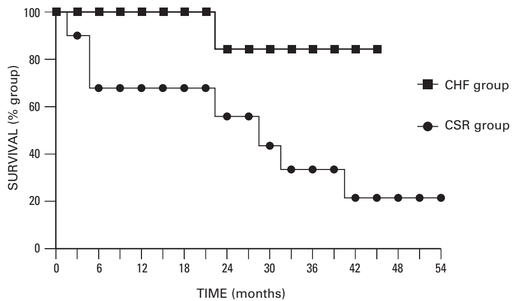
Am J Respir Crit Care Med 1996; 153(1):272-6.

Increased mortality associated with Cheyne-Stokes respiration in patients with congestive heart failure.

Hanly PJ, Zuberi-Khokhar NS.

Department of Medicine, Wellesley Hospital, University of Toronto, Canada.

We hypothesised that mortality is higher in patients with congestive heart failure (CHF) who develop Cheyne-Stokes respiration (CSR) during sleep than CHF patients without CSR. Overnight polysomnography was performed on 16 male patients with chronic, stable CHF: nine had CSR during sleep (CSR group) and seven did not (CHF group). The CSR group had a higher apnea-hypopnea index (AHI: 41 +/- 17 versus 6 +/- 5/hr) and experienced greater sleep disruption. There were no significant intergroup differences between age, weight, cardiac function, and pulmonary function. After the initial sleep study, all patients were maintained on standard medical therapy for CHF without supplemental oxygen or nasal continuous positive airway pressure. Over the next 3.1 to 4.5 years there was a significant difference between the number of deaths in each group. Five patients died in the CSR group and two received a heart transplant, whereas only one patient died in the CHF group. Regression analysis revealed that mortality was positively correlated with CSR, AHI, arousal index, and the amount of stage 1, 2 non-REM sleep and was inversely related to the total sleep time. We conclude that mortality is higher in CHF patients who develop CSR during sleep than CHF patients without CSR. Although the development of CSR may simply reflect more severe cardiac impairment, we suggest that CSR itself accelerates the deterioration in cardiac function.



Cumulative survival in the CSR and CHF groups, which was significantly lower in the CSR group (p = 0.0419).

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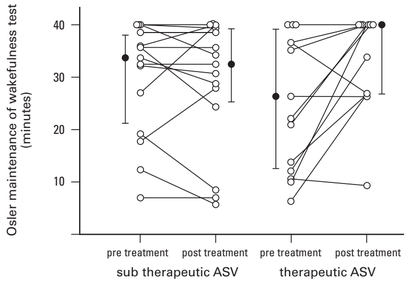
A randomised controlled trial of adaptive ventilation for Cheyne-Stokes breathing in heart failure.

Pepperell JC, Maskell NA, Jones DR, Langford-Wiley BA, Crosthwaite N, Stradling JR, Davies RJ.

Oxford Sleep Unit, Oxford Centre for Respiratory Medicine, Oxford Radcliffe Hospital, Oxford, United Kingdom. justinpepperell@doctors.org.uk

Heart failure is associated with Cheyne-Stokes breathing, which fragments patients' sleep. Correction of respiratory disturbance may reduce sleep fragmentation and excessive daytime sleepiness. This randomised prospective parallel trial assesses whether nocturnal-assist servoventilation improves daytime sleepiness compared with the control. A total of 30 subjects (29 male) with Cheyne-Stokes breathing (mean apnea-hypopnea index 19.8
[SD 2.6] and stable symptomatic chronic heart failure (New York Heart Association Class II-IV) were treated with 1 month's therapeutic (n = 15) or subtherapeutic adaptive servoventilation. Daytime sleepiness (Osler test) was measured before and after the trial with change in measured sleepiness the primary endpoint. Secondary endpoints included brain natriuretic peptide levels and catecholamine excretion. Active treatment reduced excessive daytime sleepiness; the mean Osler change was +7.9 minutes (SEM 2.9), when compared with the control, the change was -1.0 minutes (SEM, 1.7), and the difference was 8.9 minutes (95% confidence interval, 1.9-15.9 minutes; p = 0.014, unpaired t test). Significant falls occurred in plasma brain natriuretic peptide and urinary metadrenaline excretion. We conclude that adaptive servoventilation produces an improvement in excessive daytime sleepiness in patients with Cheyne-Stokes breathing and chronic heart failure. This study suggests improvements in neurohormonal activation with



Maintenance of wakefulness test (Osler test) results. Subtherapeutic adaptive servoventilation (ASV) is shown in the *left-hand columns* and therapeutic ASV is shown in the *right-hand columns*. Data are presented individually in *open circles*, with the group median and interquartile ranges also being present. Therapeutic ASV improves objective sleepiness, whereas subtherapeutic control produces no change. (Mean difference, 8.9 minutes; 95% confidence interval, 1.9–15.9; p 0.014; unpaired *t* test.)