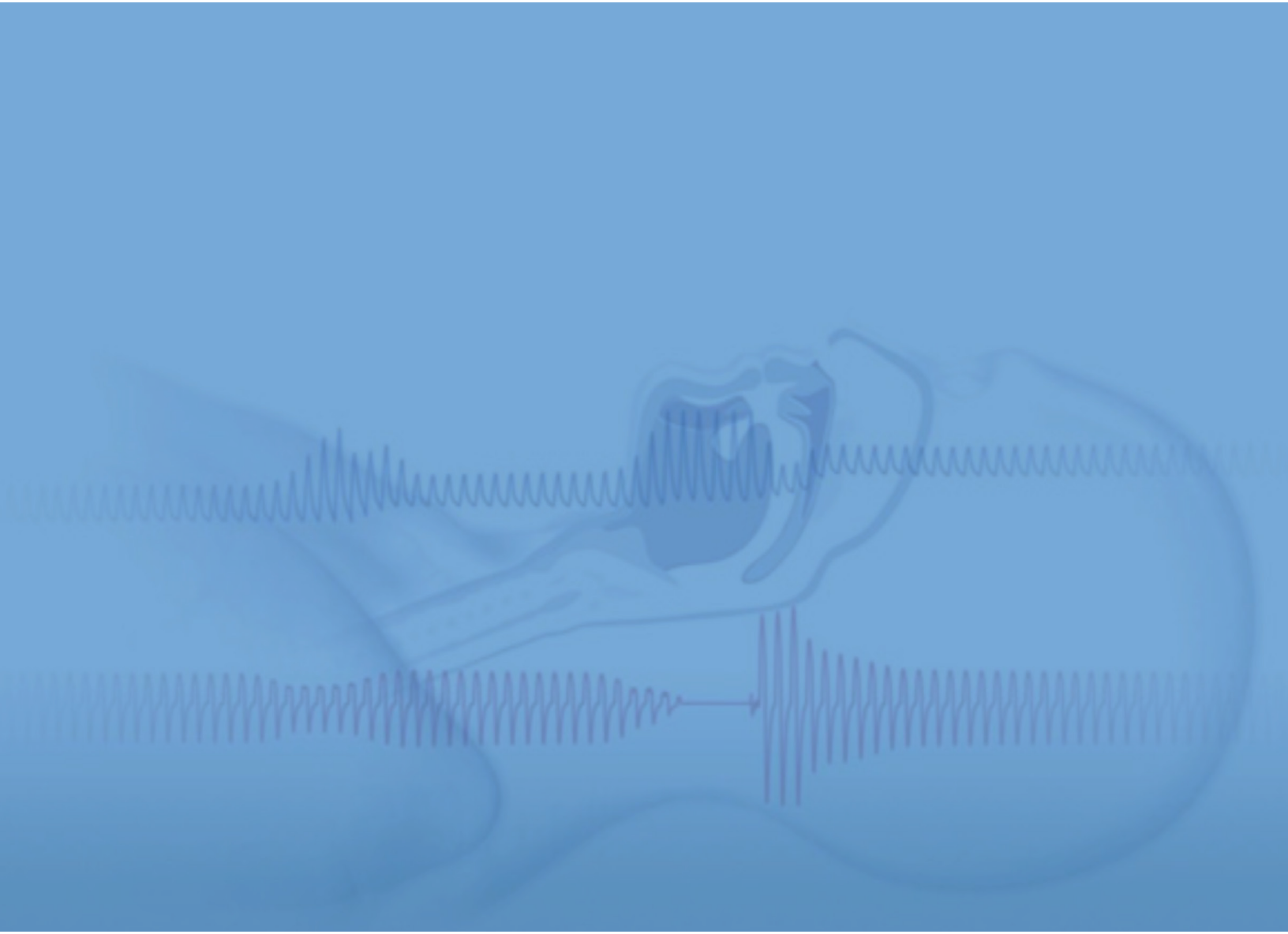




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Benefits of Adaptive Servo-Ventilation (ASV)

Clinical Abstracts
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Complex Sleep Apnea

Complex Sleep Apnea – Introduction

Complex sleep apnea (CompSA) is a form of sleep apnea where central apneas persist or emerge after the introduction of continuous positive airway pressure (CPAP) to treat obstructive sleep apnea (OSA). Approximately 5% to 15% of sleep apnea patients have been reported to have CompSA. The use of ASV therapy in CompSA has been studied in four key clinical trials which included a total of 173 patients. Results are summarized in Appendix 1.

Complex Sleep Apnea – Prevalence

Complex sleep apnea at auto-titrating CPAP initiation: prevalence, significance and predictive factors.

Neu D, Balkissou AD, Mairesse O, Pefura-Yone EW, Noseda A. *Clinical Respiratory Journal* 2015; 15 Jun [epub ahead of print]

- This retrospective cohort study assessed the prevalence of, and predictive factors for, CompSA.
- The prevalence of CompSA was 9.1% in this group of 263 patients undergoing a treatment trial with auto-titrating CPAP.
- Patients who developed CompSA during auto-CPAP had higher median apnea-hypopnea index (AHI), central apnea index (CAI) and mixed apnea index at baseline than those who did not develop CompSA, and were more likely to have comorbid heart failure and chronic obstructive pulmonary disease (COPD).

Take-home message: Up to 10% undergoing CPAP initiation develop CompSA. Patients with more severe sleep-disordered breathing at baseline and those with comorbid conditions, such as heart failure or COPD appear to be at higher risk.

A prospective polysomnographic study on the evolution of complex sleep apnea

Cassel W, Canisius S, Becker HF, Leistner S, Ploch T, Jerrentrup A, Vogelmeier C, Koehler U, Heitmann J.

European Respiratory Journal 2011;38:329-33.

- This study looked at the prevalence of complex sleep apnea (CompSA) on the first night of CPAP therapy, and the natural course of CompSA over 3 months of CPAP.
- The prevalence of CompSA on the first night of CPAP was 12.2%; patients with CompSA were significantly older than those who did not show CompSA ($p=0.001$).
- Patients with CompSA had a significantly higher AHI on the diagnostic night of CPAP than those who did not (35.9/h vs 26.2/h; $p=0.003$).

- There was a trend towards more CompSA in patients with hypertension or coronary artery disease, and less CompSA in patients with stroke.
- The prevalence of CompSA decreased significantly over three months of CPAP therapy, falling to 6.9% ($p=0.006$ vs first night of CPAP).
- Only 3.2% of patients had CompSA at both assessments.
- Patients who had CompSA at 3 months had a higher CAI and mixed apnea index on the first night of CPAP ($p<0.001$) and worse sleep quality versus those without CompSA at 3 months.

Take-home message: CompSA is not a stable phenomenon, but is instead a dynamic process. Patients with CompSA demonstrate respiratory instability even during CPAP treatment.

The prevalence and natural history of complex sleep apnea

Javaheri S, Smith J, Chung E.

Journal of Clinical Sleep Medicine 2009; 5(3):205-11.

- The aim of this retrospective study was to determine the prevalence and natural history of CPAP-emergent CompSA.
- 1286 diagnosed OSA patients who underwent titration with a positive airway device during a one-year period were included in the analysis. All patients were followed-up four weeks after CPAP initiation.
- Eighty-four patients developed a CompSA (CAI $\geq 5/h$) while on CPAP with an overall incidence of 6.5%.
- Thirty-three of 42 central sleep apnea (CSA)-emergent patients returning for a second CPAP titration, however, had CompSA eliminated within eight weeks of CPAP therapy.
- It is estimated that 1.5% of OSA patients continued to have CompSA with long-term CPAP use, with baseline CAI $\geq 5/h$, opioid use and OSA severity as potential risk factors.

Take-home message: 6.5% of OSA patients had CPAP-emergent CompSA, however CPAP-emergent CompSA is generally transitory and resolves of its own accord. Approximately 1.5% of OSA patients may have persistent CompSA with long-term CPAP use.

Prevalence of complex sleep apnea among Japanese patients with sleep apnea syndrome

Endo Y, Suzuki M, Inoue Y, Sato M, Namba K, Hasegawa M, Matsuura M.

Tohoku Journal of Experimental Medicine 2008;215:349-354.

- In this Japanese study, the overall prevalence of CompSA was 5.0% (5.3% in males and 1.1% in females).
- AHI was significantly higher in patients with CompSA versus CSA or OSA, but there were no other statistically significant differences between these patient groups (e.g. age, body mass index, cardiovascular comorbidities).

Take-home message: The prevalence of CompSA in this Japanese population was lower than that previously reported in US or Australian studies.

Complex sleep apnea syndrome: is it a unique clinical syndrome?

Morgenthaler TI, Kagramanov V, Hanak V, Decker PA.

Sleep 2006;29(9):1203-1209.

- This study determined the prevalence of CompSA in patients referred to the Mayo Clinic for polysomnography (PSG) in January 2004; patients with congestive heart failure or left ventricular dysfunction were excluded.
- The prevalence of CompSA was 15%.
- The only demographic feature that differed significantly between patients with CompSA vs OSA or CSA was male sex (81% vs 60% vs 43%, respectively, $p=0.027$).
- Patients with CompSA or CSA had a higher AHI than those with OSA ($p<0.05$ for both comparisons).
- CompSA patients showed disturbed sleep, with an AHI of 32.3/h and an arousal index of 42.1/h.
- CPAP was associated with resolution of OSA, but only partially resolved CSA and CompSA.

Take-home message: Patients with CompSA are relatively similar to those with OSA, but show a different response to CPAP, during which those with CompSA continue to have disrupted breathing and sleep.

Complex Sleep Apnea – Treatment with ASV

Clinical impact of adaptive servoventilation compared to other ventilatory modes in patients with treatment-emergent sleep apnea, central sleep apnea and Cheyne-Stokes respiration

Correia S, Martins V, Sousa L, Moita J, Teixeira F, Dos Santos JM.

Revista Portuguesa Pneumologia 2015;21(3):132-7.

- This small, non-randomized, single-center case review reported on the use of ASV for the treatment of CompSA compared with other forms of positive airway pressure (PAP).
- Over a mean follow-up period of 25 months, compliance was similar in patients treated with ASV ($n=16$) or PAP ($n=15$).
- Epworth Sleepiness Scale (ESS) scores were also similar in the ASV and CPAP groups (6 ± 5 and 7 ± 5 , respectively), while the residual AHI was lower in the ASV group ($4\pm 3/h$ vs $9\pm 3/h$; $p=0.005$).
- There was one case of acute coronary syndrome and one of progressive heart failure in the PAP group, and one episode of arrhythmias and two cases of worsening

heart failure in the ASV group; there were two episodes of sudden cardiac death in patients being treated with other PAP devices but none in those who were treated with ASV.

- However, there was no effort made to account for multiple confounding variables, and numbers were very small, making it impossible to draw any definitive conclusions from these data with respect to cardiovascular safety.

Take-home message: ASV is an efficient treatment for CompSA, with good compliance to therapy and improved sleepiness.

The complex sleep apnea resolution study: a prospective randomized controlled trial of continuous positive airway pressure versus adaptive servoventilation therapy

Morgenthaler TI, Kuzniar TJ, Wolfe LF, Willes L, McLain WC 3rd, Goldberg R.

Sleep 2014 May 1;37(5):927-34.

- This multicenter, randomized, prospective trial compared clinical and PSG outcomes during treatment of CompSA with ASV compared with CPAP.
- Treatment with ASV and CPAP for 90 days significantly reduced the ESS score from baseline.
- After two nights of titration, AHI was 5.7/h in ASV recipients versus 14.1/h in CPAP recipients ($p \leq 0.0003$). Corresponding values after 90 days of treatment were 4.4/h and 9.9/h ($p = 0.0024$).
- The CAI after titration was 1.1/h with ASV and 8.8/h with CPAP ($p \leq 0.0003$), and after 90 days was 0.7/h vs 4.8/h, respectively ($p < 0.0001$).
- The proportion of patients with successful treatment (AHI $< 10/h$) after 90 days' therapy was 89.7% in the ASV group and 64.5% in the CPAP group ($p < 0.0214$).

Take-home message: ASV significantly improves daytime sleepiness in patients with CompSA, and is more effective than CPAP for reducing the AHI and CAI.

Analysis of cardiopulmonary coupling to assess adaptive servo-ventilation success in complex sleep apnea management

Ramar K, Desruets B, Ramar P, Morgenthaler TI.
Sleep & Breathing 2013;17(2):861-6.

- Data from 106 patients with CompSA treated with ASV were analyzed in this retrospective analysis.
- ASV was successful in 81.1% of patients (AHI decreased to $< 10/h$).
- The AHI was reduced from 36.5/h to 11.0/h during ASV therapy.

Take-home message: ASV is an effective treatment in patients with CompSA.

A retrospective case series of adaptive servoventilation for complex sleep apnea

Brown SE, Mosko SS, Davis JA, Pierce RA, Godfrey-Pixton TV.
Journal of Clinical Sleep Medicine 2011; 7(2):187-95.

- The aim of this retrospective study was to examine the efficacy of ASV in PAP-refractory CSA patients.
- Twenty-five PAP-refractory CSA patients (AHI: $48.5 \pm 30.2/h$; CAI: $10.8 \pm 16.0/h$) underwent ASV titration following unsuccessful PAP titrations; 18 had CompSA.
- On ASV, AHI decreased to $11.4 \pm 8.2/h$ during titration ($p < 0.001$) and to $3.6 \pm 4.2/h$ at the optimal expiratory positive airway pressure (EPAP) ($p < 0.001$).

- AHI was $\leq 5/h$ in 80% of patients and $< 10/h$ in 92%. At optimal EPAP, ASV virtually eliminated central apneas ($0.7 \pm 2.2/h$, $p < 0.001$).
- Respiratory arousals were significantly reduced from baseline in patients treated with ASV, but not those who received PAP therapy.
- Lowest oxygen saturation and time spent with oxygen saturation $< 90\%$ both improved significantly from baseline during ASV therapy.
- The percentage of time spent in stage 1 sleep was significantly lower during ASV therapy compared with baseline.

Take-home message: ASV is more effective than traditional PAP in treating CompSA, significantly decreasing respiratory-related arousals and AHI, and improving oxygen saturation.

Efficacy of adaptive servoventilation in treatment of complex and central sleep apnea syndromes

Allam JS, Olson EJ, Gay PC, Morgenthaler TI.
Chest 2007; 132(6):1839-46.

- The aim of this retrospective study was to assess ASV effectiveness in CompSA or CSA/Cheyne-Stokes respiration (CSR).
- One-hundred patients with CompSA (63%), CSA (22%) and CSR (15%) underwent ASV titration. PSG data from patients from diagnostic studies, CPAP, bi-level and ASV titrations were compared.
- Median AHI was 48/h at baseline, 31/h during optimal CPAP titration, 15/h during optimal bilevel titration and 5/h during ASV ($p < 0.0001$ for ASV vs others).
- ASV treatment was successful (AHI $< 10/h$) in 64% of patients.
- Optimally-titrated ASV significantly increased the proportion of REM sleep (18%) compared to baseline and CPAP (12% and 10% respectively, $p < 0.0001$).
- 84% of patients contacted for follow-up information maintained ASV therapy compliance. Of these ASV-compliant patients, subjective sleep quality and daytime sleepiness were improved in 72% and 56%, respectively.

Take Home Message: The majority of patients compliant with ASV therapy have improvements in subjective sleep quality and/or daytime sleepiness. ASV effectively treats CompSA and CSA/CSR compared with other forms of PAP.

Additional References

Prevalence and treatment of central sleep apnea emerging after initiation of continuous positive airway pressure in patients with obstructive sleep apnea without evidence of heart failure.

Westhoff M, Arzt M, Litterst P.
Sleep & Breathing 2012; 16(1):71-8.

Adaptive pressure support servoventilation: a novel treatment for residual sleepiness associated with central sleep apnea events.

Su M, Zhang X, Huang M, Ding N.
Sleep & Breathing 2011; 15(4):695-9.

Comparison of two servo ventilator devices in the treatment of complex sleep apnea.

Kuzniar TJ, Patel S, Nierodzik CL, Smith LC.
Sleep Medicine 2011; 12(6):538-41.

Association between residual sleepiness and central sleep apnea events in patients with obstructive sleep apnea syndrome.

Yao SM, Zhang XL.
Chinese Journal of Tuberculosis and Respiratory Diseases 2008; 31(9):664-9.

Adaptive servoventilation versus noninvasive positive pressure ventilation for central, mixed, and complex sleep apnea syndromes.

Morgenthaler TI, Gay PC, Gordon N, Brown LK.
Sleep 2007; 30(4):468-75.

Sleep Apnea Associated with Chronic Opioid Therapy

Introduction

Long-term opioid therapy has been associated with a high prevalence of sleep-disordered breathing (SDB), with studies showing that up to 75% of opioid therapy patients have at least mild SDB (AHI $\geq 5/h$), which is predominantly central in nature. Treatment with ASV has shown to be successful in these patients, with five trials on 112 patients demonstrating that ASV significantly reduced AHI compared with control or baseline. Findings are summarized in Appendix 2.

Prevalence

Sleep disordered breathing and chronic respiratory failure in patients with chronic pain on long term opioid therapy

Rose AR, Catcheside PG, McEvoy RD, Paul D, Kapur D, Peak E, Vakulin A, Antic NA.
Journal of Clinical Sleep Medicine 2014 Aug 15;10(8):847-52.

- This study determined the prevalence and type of SDB in long-term opioid therapy recipients.
- Twenty-four patients on long-term opioids (≥ 6 months) for chronic pain underwent PSG and the results were compared with those from matched patients not receiving opioids who were referred for PSG to evaluate SDB.
- Of the chronic opioid recipients, 71% had moderate SDB (AHI $\geq 15/h$) and 46% had severe SDB (AHI $> 30/h$).

- SDB severity in opioid recipients (mean AHI 32.7/h) was similar to that in SDB patients referred for PSG (mean 28.9/h).
- Chronic pain patients receiving long-term opioids also had impaired psychomotor vigilance, which may be related to the use of opioids other centrally-acting agents and/or SDB.

Take Home Message: Patients receiving long-term opioid therapy often have SDB that is frequently central in origin, and have impaired psychomotor vigilance.

Sleep-disordered breathing and chronic opioid therapy

Webster LR, Choi Y, Desai H, Webster L, Grant BJ.
Pain Medicine 2008; 9(4):425-32.

- This study assessed the relationship between opioid use for chronic pain and SDB.
- One-hundred-and-forty patients using opioid therapy on a 24-hour basis for chronic pain over a period of ≥ 6 months completed PSG testing.
- SDB (AHI $\geq 5/h$) was present in 75% of patients; 39% were diagnosed with OSA, 24% with CSA, 8% with both OSA and CSA, and 4% had an indeterminate form of SDB.
- Correlations were noted between methadone dosage and AHI ($p=0.002$), as well as between CAI and methadone and benzodiazepine daily dosages ($p=0.008$ and 0.004 , respectively).

Take Home Message: SDB is common in patients using long-term opioids for chronic pain, with higher dosages of some opioids increasing AHI and CAI. Close monitoring of these patients and their opioid use is recommended.

Central sleep apnea in stable methadone maintenance treatment patients

Wang D, Teichtahl H, Drummer O, Goodman C, Cherry G, Cunningham D, Kronborg I.
Chest 2005; 128:1348-56.

- The prevalence of CSA in methadone maintenance treatment (MMT) patients was assessed in this study, along with possible contributors to the occurrence of CSA.
- 45 MMT patients and 20 age-, sex- and body mass index-matched controls were included; all underwent PSG, blood toxicology and assessment of ventilator responses to hypoxia and hypercapnia.

- A CAI of >5/h was recorded in 30% of MMT patients, and 20% of patients had a CAI of >10/h; normal subjects all had a CAI of <1/h.
- The obstructive apnea index was similar in MMT patients and controls.
- Methadone blood concentration was the only variable significantly associated with the severity of CAI (t=2.33, p=0.025).
- Other physiological variables identified that may play a role in the development of CAI in MMT patients were carbon dioxide pressure while awake, antidepressant use, reduced ventilatory response to hypercapnia, and widened awake alveolar-arterial oxygen pressure gradient.

Take Home Message: The prevalence of CSA in stable MMT patients is 30%, and methadone blood concentrations are significantly associated with the severity of CSA.

Sleep Apnea Associated with Chronic Opioid Therapy – Treatment with ASV

A novel adaptive servoventilation (ASVAuto) for the treatment of central sleep apnea associated with chronic use of opioids

Cao M, Cardell CY, Willes L, Mendoza J, Benjafeld A, Kushida C.

Journal of Clinical Sleep Medicine 2014 Aug 15;10(8):855-61.

- This study compared the efficacy and patient comfort of ASV versus bilevel with back-up respiratory rate (bilevel-ST) in patients with CSA associated with chronic opioid use.
- A total of 18 consecutive patients who had been receiving opioids for ≥ 6 months were prospectively enrolled and randomized to crossover treatment with ASV then bilevel-ST or vice versa.
- Both the AHI and the CAI were significantly lower during ASV treatment compared with bilevel-ST (2.5/h vs 16.3/h [p=0.0005] and 0.4/h vs 9.4/h [p=0.0002], respectively).
- The proportion of patients who had normalized respiratory parameters was 83.3% during ASV and 33.3% during bilevel-ST.
- Scores on the Morning After Patient Satisfaction Questionnaire showed that patients felt more awake after ASV versus bilevel-ST treatment (p=0.0337).

- In the absence of long-term randomized controlled trial data and guidelines, the authors recommended ASV therapy for the treatment of CSA associated with chronic opioid use.

Take-home message: ASV is superior to bilevel-ST for improving alertness and normalizing respiratory parameters in chronic opioid recipients with CSA.

Adaptive servoventilation for treatment of opioid-associated central sleep apnea

Javaheri S, Harris N, Howard J, Chung E.

Journal of Clinical Sleep Medicine 2014 Jun 15;10(6):637-43.

- The aim of this study was to determine the acute efficacy and prolonged use of ASV as treatment for CSA in patients receiving chronic opioid therapy for whom titrated CPAP therapy had failed to eliminate central apneas.
- Twenty patients underwent a night of ASV titration. Seventeen patients were followed for a minimum of nine months and up to six years. Mean long-term adherence was 5.1 ± 2.5 h/night.
- One night of ASV reduced the AHI from 61/h at baseline to 11/h (p=0.0001), the CAI from 32/h to 0/h (p=0.0004), and the arousal index from 29/h to 12/h (p=0.002).

- Minimum oxygen saturation improved from 83% at baseline to 90% during ASV ($p=0.001$).

Take-home message: ASV is effective for the treatment of CSA in patients receiving opioid therapy and long-term adherence is good.

Adaptive servoventilation (ASV) in patients with sleep disordered breathing associated with chronic opioid medications for non-malignant pain.

Farney RJ, Walker JM, Boyle KM, Cloward TV, Shilling KC. *Journal of Clinical Sleep Medicine* 2008; 4(4):311-9.

- The aim of this retrospective analysis was to assess the efficacy of ASV treatment in patients with SDB complicated by chronic opioid therapy.
- Twenty-two patients referred for evaluation of sleep apnea who were found to have an AHI ≥ 20 /h, had been using opioid therapy for ≥ 6 months and had undergone ASV testing were included in the analysis.
- ASV had no significant effect on the sleep profile or oxygenation parameters.
- The obstructive apnea index decreases significantly during ASV therapy (from 25.8/h at baseline to 2.4/h; $p < 0.0001$); the decrease in mean CAI from 26.4/h to 15.6/h was not statistically significant ($p = 0.127$).

Take-home message: Overall, ASV was considered to be insufficient. Residual obstructive and central events with ASV treatment may be attributed to suboptimal pressure settings and pathophysiological and ataxic breathing, respectively.

Adaptive pressure support servoventilation: a novel treatment for sleep apnea associated with use of opioids

Javaheri S, Malik A, Smith J, Chung E.

Journal of Clinical Sleep Medicine 2008; 4(4):305-10.

- The aim of the study was to investigate PAP methods for treating SDB related to chronic opioid use.
- Five patients using chronic opioid therapy underwent baseline PSG (AHI 70/h), followed by CPAP and ASV titration.
- ASV AHI at final therapy pressures (13/h) was significantly reduced compared with that during optimal CPAP titration (42/h, $p = 0.04$).
- CAI on ASV (0/h) was significantly reduced compared to CPAP (37/h, $p = 0.01$).
- ASV also significantly improved the arousal index (62 ± 18 to 24 ± 9 /h, $p = 0.02$) and respiratory disturbance index (RDI; 58 ± 17 to 16 ± 7 /h, $p = 0.01$) compared with baseline.

Take home message: In patients with SDB related to chronic opioid therapy, ASV is the most effective form of PAP treatment for reducing arousals, the RDI, and obstructive and central apneas.

Additional References

Obstructive sleep apnea is more common than central sleep apnea in methadone maintenance patients with subjective sleep complaints.

Sharkey KM, Kurth ME, Anderson BJ, Corso RP, Millman RP, Stein MD.

Drug and Alcohol Dependence 2010;108(1-2):77-83.

Other Central Apnea Indications: Treatment with ASV Idiopathic CSR – Treatment with ASV

Adaptive servo-ventilation in patients with idiopathic Cheyne-Stokes breathing

Banno K, Okamura K, Kryger MH.

Journal of Clinical Sleep Medicine 2006; 2(2):181-6.

- The aim of the study was to investigate ASV for treatment of CSR not associated with heart failure or other serious medical issues.
- Three patients with idiopathic daytime and nocturnal CSR were tested on CPAP and/or oxygen but did not respond well.

- ASV treatment reduced the abnormal events index from 35.2/h to 3.5/h.
- There was also a significant reduction in the number of arousals (18.5/h to 1.1/h).
- Follow-up at six to 12 months showed a significant improvement in sleep quality, daytime alertness, concentration and mood in ASV recipients.

Take home message: ASV normalizes sleep-related breathing events and improves sleep quality, daytime alertness, concentration and mood In patients with idiopathic CSR.

Stroke and CSA –Treatment with ASV

Adaptive servo-ventilation as treatment of persistent central sleep apnea in post-acute ischemic stroke patients

Brill AK, Rösti R, Hefti JP, Bassetti C, Gugger M, Ott SR. *Sleep Medicine* 2014 Aug 1 [Epub ahead of print].

- This single-centre retrospective study evaluated the role of ASV in the treatment of persistent CSA in patients who had experienced an acute ischemic stroke.
- Fifteen patients were treated with ASV; initial treatment with CPAP (n = 11) or bilevel PAP (n=2) had been ineffective at controlling CSA.
- Mean ASV usage was 5 hours 20 minutes per night at three months and 6 hours 22 minutes per night at six months.

- ASV also improved daytime sleepiness, with a decrease in the ESS score from 8.6 at baseline to 5.6 during ASV ($p=0.08$). In patients who used ASV for ≥ 5 h/night, the ESS score decreased from 9.0 at baseline to 4.2 ($p=0.028$).
- AHI was 46.7/h at baseline, and was reduced to 8.5/h ($p=0.001$) and 10.7/h ($p=0.024$) after three and six months of ASV, respectively.
- ASV was generally well tolerated and no severe side effects were reported.

Take-home message: ASV improves daytime sleepiness in post-acute stroke patients, especially when used for ≥ 5 h/night, and is a feasible and well tolerated treatment option.

CSA of Various Etiologies –Treatment with ASV

Effectiveness of Adaptive Servo Ventilation in the treatment of hypocapnic central sleep apnea of various etiologies

Carnevale C, Georges M, Rabec C, Tamisier R, Levy P, Pépin JL.

Sleep Medicine 2011;12(10):952-8.

- Outcomes for 74 patients with CSA treated with ASV for a mean of 36 months were described in this retrospective chart review .
- CSA was associated with neurological disorders or had an idiopathic origin in 41 patients, and the remaining 33 had CSA related to heart failure.

- Mean ASV usage was 5–6 hours/night.
- Mean AHI decreased from 47.4 ± 19.8 at baseline to 6.9 ± 9.3 /h during ASV ($p < 0.001$),
- Nocturnal oxygen saturation increased from $92.1 \pm 2.6\%$ to $93.6 \pm 3.2\%$ ($p < 0.001$).
- ASV significantly reduced chronic hyperventilation as shown on blood gas analysis ($p < 0.05$).
- Daytime sleepiness was significantly improved during ASV therapy, as indicated by a reduction in the ESS score from 10.2 ± 5.2 at baseline to 6.5 ± 3.9 ($p < 0.01$).

Take-home message: ASV is effective and well tolerated for the majority of patients with hypocapnic CSA and chronic hyperventilation.

Post-surgery use of ASV

Efficacy of cardiopulmonary rehabilitation with adaptive servo-ventilation in patients undergoing off-pump coronary artery bypass grafting

Tashiro N, Takahashi S, Takasaki T, Katayama K, Taguchi T, Watanabe M, Kurosaki T, Imai K, Kimura H, Sueda T.

Circulation Journal 2015;79(6):1290-8.

- This study aimed to evaluate the efficacy of cardiopulmonary rehabilitation with ASV in 66 patients undergoing off-pump coronary artery bypass grafting; ASV was used from postoperative day one through five in 30 patients, while the remaining 36 did not receive ASV (non-ASV).

- ASV was associated with significant reductions in systolic and diastolic blood pressure compared with non-ASV patients ($p=0.0006$ and $p=0.0277$, respectively).
- The incidence of AF was 10% in the ASV group compared with 33% in the non-ASV group ($p=0.0377$).
- Use of ASV was also associated with significant reductions in the duration of oxygen inhalation and post-operative hospitalization ($p=0.0238$ and $p=0.0392$ vs non-ASV, respectively).

Take-home message: Use of ASV therapy after off-pump coronary artery bypass grafting decreased blood pressure, the rate of atrial fibrillation, the duration of oxygen therapy and time spent in hospital.

Adaptive-servo ventilation combined with deep sedation is an effective strategy during pulmonary vein isolation

Murakami T, Yamaji H, Numa K, Kawamura H, Murakami M, Higashiya S, Kamikawa S, Hina K, Hirohata S, Kusachi S. *Europace* 2013;15(7):951-6.

- The effects of ASV in combination with deep propofol sedation on pulmonary vein isolation (PVI) using a NavX in patients with atrial fibrillation (AF) were determined in this study and compared with a control group of patients who underwent PVI without ASV.

- Compared with those who did not have ASV, patients in the ASV group had a significantly lower frequency of respiratory compensation ($p < 0.05$) and EnGuide alignment of catheter position by the NavX ($p < 0.01$), and required a significantly lower total electrical energy supply ($p < 0.01$).
- Fluoroscopy and procedure times were significantly shorter in the ASV versus non-ASV group, and the rate of recurrent AF was significantly lower (12% vs 25%; $p < 0.01$).

Take-home message: ASV facilitates successful PVI for AF and reduces the rate of recurrent AF.

Complex insomnia and SDB – Prevalence and treatment with ASV

A two-year prospective study on the frequency and co-occurrence of insomnia and sleep-disordered breathing symptoms in a primary care population

Krakow B, Ulibarri VA, Romero EA, McIver ND. *Sleep Medicine* 2013;14(9):814-23.

- The aim of this study was to evaluate the frequency and co-occurrence of insomnia and SDB symptoms, and potential co-morbidity (complex insomnia).
- A prospective self-assessment was conducted for adult patients with no prior sleep issues who presented to community-based primary care clinics for nonsleep-related complaints between November 2009 and June 2012; a brief sleep health survey (SHS) assessed insomnia and SDB symptoms.
- Of 801 patients, 660 (82.4%) reported at least one insomnia symptom, and 289 (36.1%) reported an insomnia disorder (Insomnia Severity Index [ISI] > 7 and self-reported daytime impairment due to insomnia).
- At least one SDB symptom was reported by 478 (59.7%) patients, and 177 (22.1%) reported two or more symptoms.
- Co-occurrence of insomnia and SDB symptoms occurred in 50.8% of subjects.
- Using liberal criteria to assess potential co-morbid disorders (complex insomnia), 187 (23.4%) patients reported an insomnia disorder and at least one SDB symptom.
- With more stringent criteria, including only patients with moderate or severe insomnia disorders plus two SDB symptoms, 48 patients (6.0% of the sample or 16.6% of all patients with insomnia disorders) indicated potential complex insomnia.

Take-home message: Co-occurrence of insomnia and SDB symptoms is common, as is the rate of potential complex insomnia.

Prevalence of sleep breathing complaints reported by treatment-seeking chronic insomnia disorder patients on presentation to a sleep medical center: a preliminary report

Krakow B, Ulibarri VA.

Sleep and Breathing 2013;17(1):317-22.

- This study evaluated self-report of SDB in treatment-seeking chronic insomnia patients seeking treatment at a private, community-based sleep medical center ($n = 1035$).
- The proportion of patients who ranked a sleep breathing disorder among their list of reasons for seeking treatment was 42%, with another 13% reporting concern about a sleep breathing problem and 26% reporting awareness of sleep breathing symptoms; only 19% of the study population reported no awareness of or concerns about sleep breathing disorders, problems, or symptoms.
- A greater proportion of men than women reported significantly more sleep breathing disorders, problems, or symptoms.

Take-home message: A very high proportion of patients seeking treatment for chronic insomnia report a sleep breathing disorder (81%).

Adaptive Servo-Ventilation therapy in a case series of patients with co-morbid insomnia and sleep apnea

Krakow B, Ulibarri VA, Romero E, Thomas RJ, McIver N.
Journal of Sleep Disorders: Treatment and Care 2013;2:1.

- Chart review was conducted to determine the effects and use of ASV therapy in 56 insomnia patients with co-morbid SDB (complex insomnia) who failed standard PAP therapy.
- Compared to standard PAP, ASV significantly improved objective breathing event indices.
- ASV increased sleep efficiency, proportion of sleep time spent in REM, and REM sleep consolidation, and decreased awakenings, arousals, and time awake during the night.
- Among 39 of 43 current ASV users, adherence was significantly greater (both nightly use and hours per night) compared to prior use of standard PAP.

Take-home message: ASV improves breathing and sleep quality in patients with insomnia and SDB. Adherence to PAP therapy in these patients is better than to standard PAP.

Adaptive pressure support servoventilation: a novel treatment for residual sleepiness associated with central sleep apnea events

Su M, Zhang X, Huang M, Ding N.
Sleep and Breathing 2011 Dec;15(4):695-9.

- This study used the ESS to evaluate the efficacy of ASV for treating residual sleepiness (RS) in obstructive sleep apnea hypopnea syndrome (OSAHS) patients with RS after one month of auto CPAP treatment (n=42). Patients also underwent PSG.
- After one week of ASV treatment, RS patients had significant reductions in the AHI, CAI, mixed apnea index, arousal index, and daytime ESS score compared with the end of CPAP (all $p < 0.0001$); mean and minimum oxygen saturation were significantly increased ($p < 0.0001$ vs end of CPAP).
- The ESS score decreased from 10.89 ± 0.40 before ASV to 3.98 ± 1.26 on day seven of ASV treatment (i.e. to within the normal range).

Take-home message: ASV significantly improves RS in OSAHS patients who did not respond to CPAP.

Appendix I – Summary of key findings for studies investigating ResMed ASV for SDB in patients with complex sleep apnea

Author (date)	N (ASV)	ASV duration	Clinical outcomes associated with ASV therapy
Correia (2015)	16	Mean 25 months	Compliance with treatment was good. ESS score was low (mean 6) indicating good daytime alertness.
Brill (2014)	15	6 months	Treatment success (AHI <10/h) was reported in 89.7% of patients. Daytime sleepiness was significantly improved vs baseline.
Morgenthaler (2014)	33	90 days	Treatment success (AHI <10/h) was reported in 89.7% of patients. ASV was more effective than CPAP at reducing the AHI and CAI. ESS score was significantly reduced vs baseline.
Ramar (2013)	106	-	Treatment success (AHI <10/h) was reported in 81.1% of patients.
Brown (2011)	25	1 night	Treatment success (AHI <10/h) was reported in 92% of patients. Respiratory arousals and time spent in stage 1 sleep were significantly reduced. Lowest oxygen saturation and time spent with oxygen saturation <90% significantly improved from baseline.
Allam (2007)	100	1 night	Treatment success (AHI <10/h) was reported in 64% of patients. Optimally-titrated ASV significantly increased the proportion of REM sleep (18%) vs baseline and CPAP. Compliance was good during long-term follow-up. Over long-term follow-up, subjective sleep quality and daytime sleepiness were improved in 72% and 56% of ASV-compliant patients, respectively.

AHI, apnea-hypopnea index; ASV, Adaptive Servo-Ventilation; CAI, central apnea index; CPAP, continuous positive airway pressure; ESS, Epworth Sleepiness Scale.

Appendix 2 – Summary of key findings for studies investigating ResMed ASV for SDB in patients receiving chronic opioid therapy

Author (date)	N (ASV)	SDB pattern	Duration of opioid therapy	ASV duration	Clinical outcomes associated with ASV therapy
Cao (2014)	18	CSA (CAI ≥5/h)	≥6 months	1 night	Respiratory parameters were normalized in 83.3% vs 33.3% of patients in the ASV vs control group, respectively. Patients felt significantly more awake after ASV.
Javaheri (2014)	20	CSA (CAI ≥5/h)	“Chronic”	1 night	ASV improved the AHI, CAI and oxygen saturation vs baseline Long-term adherence was good (mean 5.1 h/night).
Farney (2008)	22	CSA	≥6 months	NR	ASV had no effect on the sleep profile or oxygenation parameters. Treatment was considered to be insufficient.
Javaheri (2008)	5	SDB	2-5 years	1 night	ASV was more effective than CPAP at reducing arousals and the respiratory disturbance index.

AHI, apnea-hypopnea index; BMI, body mass index; CAI, central apnea index; CompSA, complex sleep apnea; CPAP, continuous positive airway pressure; CSA, central sleep apnea; NR, not reported.

Note: ASV therapy is contraindicated in patients with chronic, symptomatic heart failure (NYHA 2-4) with reduced left ventricular ejection fraction (LVEF ≤ 45%) and moderate to severe predominant central sleep apnea.