Management of Complicated Sleep Apnea

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Learning Objectives

- Define complicated sleep disordered breathing
- Identify etiologic mechanisms
- Describe the natural history of complex sleep apnea
- Recognize the uses and limitations of ASV and AVAPS

Polysomnography

Mode	Total AHI	OA	OH	CA
Baseline	141	26	188	77
CPAP 5	137	14	53	33
CPAP 7	124	10	25	11
CPAP 9	46	1	15	1
CPAP 11	63	4	17	23
CPAP 11 + 2L	97	3	5	26
BPAP 15/11	68	5	4	31

Management of CompSA

- Continue CPAP
  - Lower setting
  - Trial of higher setting
  - Add O2
- Stop CPAP, repeat PSG within a few days
- Switch to BPAP ± O2 ± back-up rate
- Switch to ASV

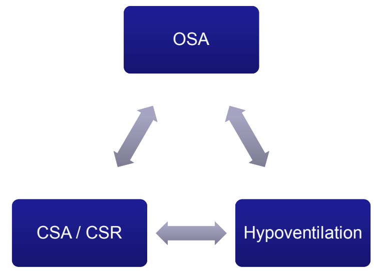
Patients

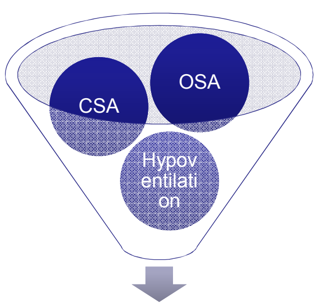
- 44, F, healthy, snoring, in Denver
- 68, M, heart failure, dyspnea
- 25, M, chronic pain, on narcotics

Patients

- 71, M, stroke, limited mobility
- 59, M, obese, snoring + apneas
- 69, F, snoring, insomnia, anxiety

Sleep Disordered Breathing





Complicated Sleep Apnea

Syndrome Complexes

OSA + CSA	Heart failure Complex sleep apnea
OSA + Hypoventilation	COPD
CSA + OSA + Hypoventilation	Opioids Neuromuscular disorder Stroke

CSA: Classification

- Hypercapnic
- Non-hypercapnic
  - Cheyne Stokes

Hypercapnic CSA

Clinical Features	**Causes**
High sleep PaCO2 Often associated with high waking PaCO2 Decreased ventilatory responsiveness to hypercapnia	Neuromuscular disorders Chronic use of long-acting opioids

Non-hypercapnic CSA

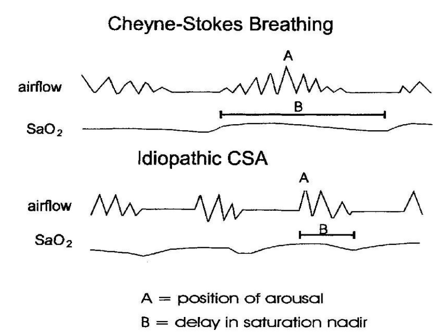
Clinical Features	Causes
Normal or low waking PaCO2 Increased ventilatory response to hypercapnia Brief arousals during sleep trigger a ventilatory "overshoot" that lowers PaCO2 below its apneic threshold	Idiopathic CSA Sleep-onset CSA CSA due to HF High altitude periodic breathing Complex sleep apnea

CSA vs. Cheyne Stokes

	CSA	CSR
Cycle time	Shorter (< 45 seconds)	Longer (> 45 seconds)
Period of hyperpnea	Shorter	Longer

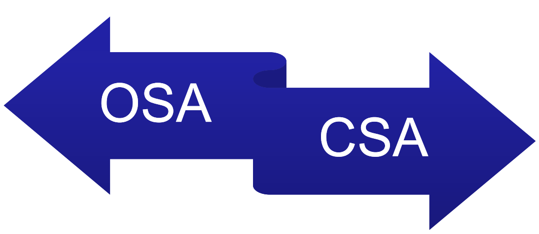
CSA vs. Cheyne Stokes

	CSA	CSR
Nadir of O2 desaturation	Following termination of apnea	More delayed
Timing of arousals	Termination of apnea	Peak of hyperpnea



Berry R, Sleep Medicine Pearls

Heart Failure



Nocturnal rostral fluid shift: a unifying concept for the pathogenesis of obstructive and central sleep apnea in men with heart failure.
Yumino D et al. *Circulation. 2010 Apr 13;121(14):1598-605.*

- Question: Does overnight rostral fluid displacement and subsequent increase in neck circumference affect the severity of OSA and CSA in HF?
- Subjects: 57 subjects with HF (EF ≤ 45%)
- Methods: Prospective observational study
  - Subjects were divided into 2 groups:
    - Obstructive-dominant (≥ 50% of events are obstructive)
    - Central-dominant (> 50% of events are central)
  - Subjects with OSA received CPAP

Nocturnal rostral fluid shift: a unifying concept for the pathogenesis of obstructive and central sleep apnea in men with heart failure.
Yumino D et al. *Circulation. 2010 Apr 13;121(14):1598-605.*

- Methods:
  - Before and after PSG
    - Leg fluid volume (bio-electrical impedance)
    - Neck circumference
  - During PSG
    - TcCO2

Nocturnal rostral fluid shift: a unifying concept for the pathogenesis of obstructive and central sleep apnea in men with heart failure.
Yumino D et al. *Circulation. 2010 Apr 13;121(14):1598-605.*

- Outcomes:
- Among subjects in the obstructive-dominant group, overnight change in leg fluid volume was inversely related to:
  - Overnight change in neck circumference
  - AHI
  - But not TcCO2

Nocturnal rostral fluid shift: a unifying concept for the pathogenesis of obstructive and central sleep apnea in men with heart failure.
Yumino D et al. *Circulation. 2010 Apr 13;121(14):1598-605.*

- Outcomes:
- Among subjects in the central-dominant group, overnight change in leg fluid volume was inversely related to:
  - Overnight change in neck circumference
  - AHI
  - But directly related to TcCO2

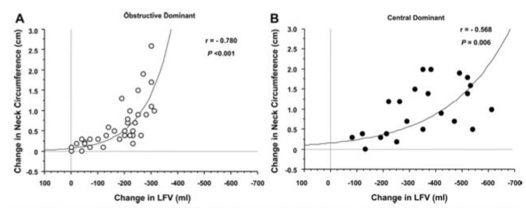


Figure 1. In both the obstructive- (A) and central-dominant (B) groups, there were inverse exponential relationships between overnight changes in neck circumference and LFV.

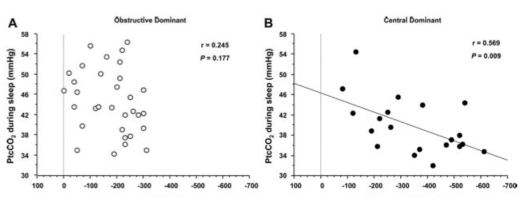


Figure 2. In the obstructive-dominant group, there was no significant correlation between mean $Ptcco_2$ during sleep and overnight change in LFV (n=32; A). However, in the central-dominant group, there was a significant correlation between mean sleep $Ptcco_2$ and the overnight change in LFV (n=20; B).

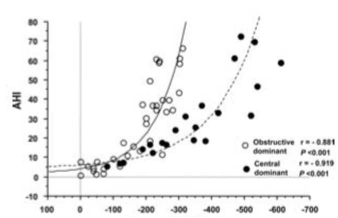


Figure 3. Relationship between change in LFV and AHI in the obstructive- and central-dominant groups. The open circles and solid line represent the relationship between the AHI and the change in LFV in the obstructive-dominant group [$y=2.4 \cdot e^{(-0.011 \cdot x)}$]. The closed circles and dashed line represent the relationship between the AHI and the change in LFV in the central-dominant group [$y=5.1 \cdot e^{(-0.004 \cdot x)}$]. The slopes of these curves differed significantly ($P<0.001$).

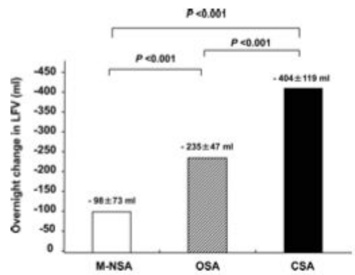
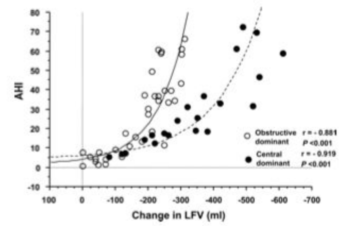


Figure 4. Demonstration of a progressively greater reduction in LFV from patients with mild to no sleep apnea (M-NSA) (AHI <15; n=19) to OSA (AHI ≥15; n=21) to CSA (AHI ≥15; n=17).



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Shift in sleep apnoea type in heart failure patients in the CANPAP trial.
Ryan CM et al. *Eur Respir J. 2010 Mar;35(3):592-7.*

- Question: Does improvement in heart function during CPAP therapy of CSA in persons with HF lead to conversion of respiratory events into obstructive apneas?
- Subjects: 98 subjects with HF and CSA
  - LVEF: < 40%
  - AHI: ≥ 15 (> 50% central apneas)

Shift in sleep apnoea type in heart failure patients in the CANPAP trial.
Ryan CM et al. *Eur Respir J. 2010 Mar;35(3):592-7.*

- Definitions:
  - Non-converter: > 50% of events remained central at follow-up
  - Converter: ≥ 50% of events were obstructive at follow-up

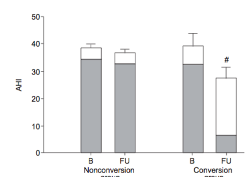


FIGURE 1. Total, central (■) and obstructive (□) apnoea/hypopnoea index

Shift in sleep apnoea type in heart failure patients in the CANPAP trial.
Ryan CM et al. *Eur Respir J. 2010 Mar;35(3):592-7.*

- Methods: Sub-analysis of the control arm of CANPAP randomized controlled trial
- Outcomes:
- Number of converters at follow-up: 18 subjects
  - 82% Non-converters
  - 18% Converters

TABLE 3 Changes in cardiovascular variables from baseline to follow-up

Variable	Nonconversion group	Conversion group	p-value
Subjects n	80	18	
ΔNYHA class	0.0 (-0.1–0.2)	-0.1 (-0.5–2.3)	0.38
ΔLVEF %	-0.7 (-1.9–0.6)	2.8 (-0.4–6.0)	0.01
ΔCHFQ dyspnoea score	0.1 (0.5–1.2)	0.9 (0.2–1.6)	0.01

Data are presented as mean (95% CI), unless otherwise indicated. ΔNYHA: change in New York Heart Association; ΔLVEF: change in left ventricular ejection fraction; ΔCHFQ: change in Chronic Heart Failure Questionnaire score (>0.75 represents important change of moderate magnitude). p-values are for between group comparisons (ANCOVA).

Complex Sleep Apnea

- Development or persistence of CSA or CSR with acute CPAP therapy in patients with predominantly OA or MA during the initial diagnostic study
- CPAP successfully eliminates OAH events but AHI remain elevated and sleep disruption persists due to CSA or CSR

Alternative Names

- CPAP-emergent CSA
- CPAP-persistent CSA
- Complicated sleep disordered breathing

- Many consider CompSA as a clinical subtype of CSA

Clinical Features

Compared to OSA	Compared to CSA
Slightly lower BMI	Higher BMI More frequent snoring Less HF Higher LVEF

Prevalence of Complex Sleep Apnea

Author/ Site (year)	n	Complex Sleep Apnea	PSG	AHI , n /hr	Follow-up PSG
Morgenthaler Rochestor, USA (06)	223	15%	Split	32	-
Derniaka Oklahoma, USA (06)	116	20%	Split	51	2%
Lehman Adelaide, Australia (07)	99	13%	Mixed	72	-
Javaheri Cincinnati, USA (09)	1286	6.5%	Full Night	57	2%
Endo Japan (07)	1232	5.3%	Full Night	59	-
Yaegashi Japan (09)	297	5.7%	Full Night	56	-

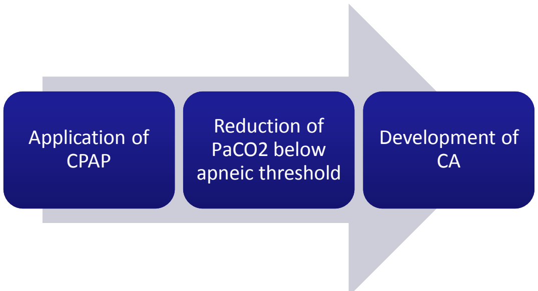
The prevalence and natural history of complex sleep apnea.
Javaheri S et al. *J Clin Sleep Med 2009;5(3):205-211.*

- Question: What is the prevalence and natural history of CPAP-emergent CSA?
- Subjects: 1286 persons with newly diagnosed OSA
- Methods: Retrospective review
- Subjects underwent a full-night attended PSG and a full-night attended CPAP titration
- A second full-night attended CPAP titration was performed 5-6 weeks later for those who developed CPAP-emergent CSA

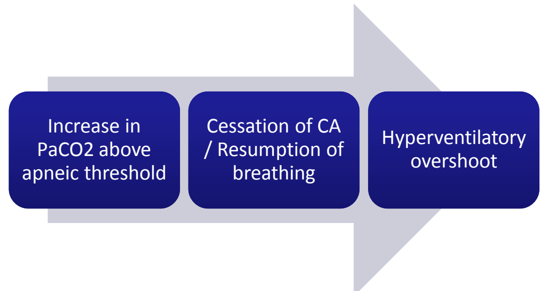
The prevalence and natural history of complex sleep apnea.
Javaheri S et al. *J Clin Sleep Med 2009;5(3):205-211.*

- Outcomes:
- Overall incidence of CPAP-emergent CSA (CAI ≥ 5) was 6.5%
- Of the 84 subjects, 42 had a second PSG, and CSA was eliminated in 33 subjects
  - Overall prevalence of CSA with long-term CPAP use was 1.5%
- Factors that were associated with persistent CPAP-emergent CSA were severe OSA, baseline CAI ≥ 5 and use of opioids

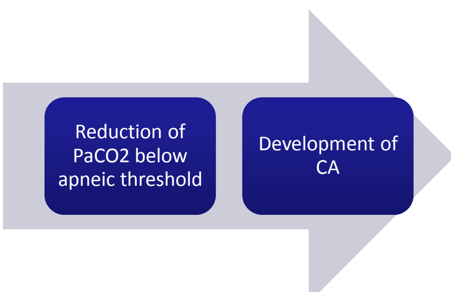
Pathophysiology

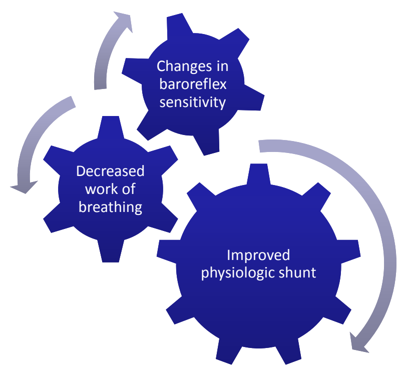


Pathophysiology



Pathophysiology





Pathophysiology

- Probability of CA developing is greater if
  - Narrow difference between baseline PaCO2 and apneic threshold (CO2 reserve)
  - Increased respiratory sensitivity to PaCO2 (controller gain)

Differential Diagnosis

- Concurrent CSA and OSA with elimination of obstructive events during CPAP titration
- Variable SRBD
  - Supine-position OA and non-supine CA
  - NREM periodic breathing and REM OA
- Acute development of anxiety with post-hyperventilatory hypocapnic CA

Management of CompSA

- Determine underlying pathophysiology
- Maximize medical therapy for comorbid disorders

Management of CompSA

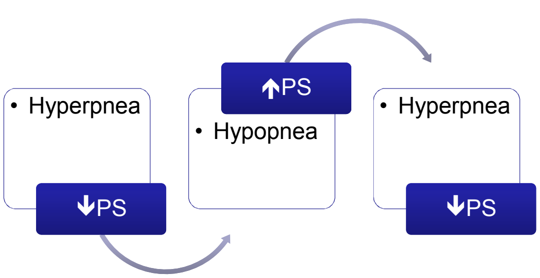
- Continue CPAP
  - Lower setting
  - Trial of higher setting
  - Add O2
- Stop CPAP, repeat PSG within a few days
- Switch to BPAP ± O2 ± back-up rate
- Switch to ASV

Servo ventilation

- Assures constant ventilation based on measurements of airflow, either:
  - Peak flow
  - Minute ventilation
- Provides varying amounts of respiratory support (above expiratory pressure) during different phases of periodic breathing

Servo ventilation

- Automatically adjusts settings in response to specific respiratory events
  - Increases EPAP for obstructive events
  - Increases inspiratory PS for hypopneas
  - Decreases inspiratory PS for hyperpneas/hyperventilation
  - Back up rate for impending apneas



Servo ventilation

- 2 types of devices:
  - BiPAP AutoSV Advanced
  - VPAP Adapt ASV Enhanced

BiPAP AutoSV Advanced

- Target: 4-minute moving average of breath-by-breath peak flow
- Settings:
  - Automatic EPAP: 4-25 cmH_2O
  - EPAP increases by 1 cmH_2O q 15 seconds for obstructive apneas/hypopneas or snoring; proactive search q 5 min
  - Automatic PS: 0 to (30 minus EPAP)
  - Automatic back-up rate: 4-30

BiPAP AutoSV Advanced

- Initial settings

– EPAPmin	4	cmH2O
– EPAPmax	15	
– Psmin	0	
– Psmax	20	
– Max pressure	25	
– Rate	Auto	
– Biflex	+/-	

BiPAP AutoSV Advanced

- If patient is unable to fall asleep
  - Adjust Biflex
  - If UA obstruction present – increase EPAPmin by 1-2 cmH2O
  - If UA obstruction absent – increase PSmin by 1-2 cmH2O

BiPAP AutoSV Advanced

- During the night
  - If obstructive events persist – increase EPAPmin
  - If central events persist – increase PSmax or set rate to minimum of 8-10 bpm

VPAP Adapt ASV Enhanced

- Target: 90% of 3-minute moving average of MV
- Settings:
  - EPAP: 4-15 cmH_2O
  - PS[min]: 3-6 cmH_2O; PS[max]: 8-16 cmH_2O
  - By manually setting EPAP, the device automatically adjusts PS[min] (3 cmH20) first then PS[max] (8 cmH20)

VPAP Adapt ASV Enhanced

- Settings:
  - PS[max] – PS[min] ≥ 5 cmH_2O
  - EPAP + PS[max] ≤ 25 cmH_2O
  - Default back-up rate: 15/min

Servo ventilation

	BiPAP	VPAP
Target	Peak flow	Minute ventilation
EPAP	Automatic	Manual
EPAP	4-25 cmH20	4-15 cmH20
PS [min]	0 cmH20	3 cmH20
Rate [default]	15	15

Adaptive servoventilation versus noninvasive positive pressure ventilation for central, mixed, and complex sleep apnea syndromes.
Morgenthaler TI et al. Sleep 2007

- Comparison of efficacy of NPPV and ASV
- Prospective RCT
- Two academic sleep programs
- 21 patients
  - CSA/CSR: 6
  - Predominantly MA: 6
  - CompSAS: 9

Adaptive servoventilation versus noninvasive positive pressure ventilation for central, mixed, and complex sleep apnea syndromes.
Morgenthaler TI et al. Sleep 2007

Inclusion criteria

- Age ≥ 18 years
- Attended CPAP titration study within 12 months

Adaptive servoventilation versus noninvasive positive pressure ventilation for central, mixed, and complex sleep apnea syndromes.
Morgenthaler TI et al. Sleep 2007

Changes in AHI

- Initial diagnostic AHI: 51.9 ± 22.8/hr
- Reduction in mean AHI
  - CPAP: 34.3 ± 25.7
  - NPPV: 6.2 ± 7.6
  - ASV: 0.8 ± 2.4 (P <0.01)

Adaptive servoventilation versus noninvasive positive pressure ventilation or central, mixed, and complex sleep apnea syndromes.
Morgenthaler TI et al. Sleep 2007

	NPPV	ASV
CSA/CSR	1.5 ± 1.5	0 ± 0
MA	10.2 ± 10.6	0.5 ± 0.8
CompSAS	6.8 ± 6.8	1.6 ± 3.6

Efficacy of adaptive servoventilation in treatment of complex and central sleep apnea syndromes.
Allam JS et al. Chest 2007

- Retrospective chart review
- First 100 patients with ASV titration
- Indications of ASV titration
  - CompSAS: 63%
  - CSA: 22%
  - CSA/CSR: 15%
- All had suboptimal response to CPAP
- Median diagnostic AHI: 48 (range 24-62)

Efficacy of adaptive servoventilation in treatment of complex and central sleep apnea syndromes.
Allam JS et al. Chest 2007

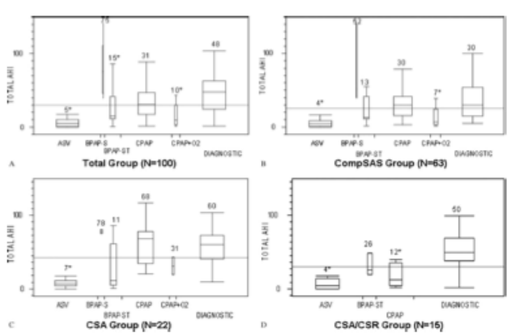
Diagnostic polysomnography

- Median AHI: 48
- Median OAI: 13
- Median CAI: 4

Efficacy of adaptive servoventilation in treatment of complex and central sleep apnea syndromes.
Allam JS et al. Chest 2007

Change in respiratory events

	CPAP	BPAP-S	BPAP-S/T	ASV
AHI:	31	75	15	5
OAI:	1	5	0	0
CAI:	16	40	1	0



If ASV Fails

- Reevaluate for underlying comorbidities
  - Maximize therapy
  - Reduce opioids
- Switch to "other" ASV device
- Increase PEEP in ASV

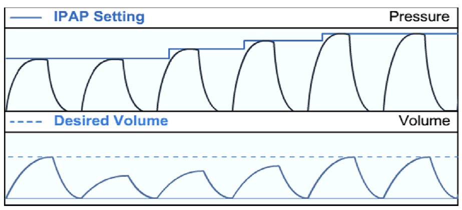
If ASV Fails

- Add oxygen
- Trial of hypnotic agents
- Trial of acetazolamide
- CO2 monitors
- Trial of NIPPV (BiPAP with AVAPS)

BiPAP with AVAPS

- Bi-level with Average Volume Assured Pressure Support (AVAPS)
  - Maintains a stable tidal volume when the patient is placed on either the S, ST or T mode
  - By automatically adjusting PS between IPAPmin and IPAPmax settings
  - Avoids breath by breath changes in IPAP levels (1 mbar/min)

BiPAP with AVAPS



Courtesy of Philips Respironics

BiPAP with AVAPS

- Indications
  - OHS
  - COPD
  - Neuromuscular weakness
  - CCHS (one case report)
  - Others requiring nocturnal ventilation?

BiPAP with AVAPS

- NOT recommended for patients with periodic breathing

BiPAP with AVAPS

- Initial settings
  - EPAP 4 cmH2O
  - IPAPmin 8
  - IPAPmax 25
  - Rate 8-10 bpm
  - I-time 1.5 sec
  - Rise time 2-3
  - Tidal volume* 8 mL/kg ideal body weight

*adjust to patient comfort to allow sleep onset

BiPAP with AVAPS

3 ways to choose a starting tidal volume with AVAPS:

1. MD suggestion
2. Patient comfort
3. Ideal body weight: 8 ml/kg*

*AVAPS suggested tidal volume settings based on height and ideal weight.

height	59"	61"	63"	65"	67"	69"	71"	73"	75"
ideal weight	52.0 kg	55.5 kg	59.0 kg	62.5 kg	66.5 kg	70.5 kg	74.5 kg	78.5 kg	83.0 kg
8 ml/kg V_T	420 ml	440 ml	470 ml	500 ml	530 ml	560 ml	600 ml	630 ml	660 ml

Courtesy of Philips Respironics

BiPAP with AVAPS

- During the night
  - If obstructive events persist – increase EPAP and IPAPmin (maintain PS)
  - If hypoventilation persists – increase PS or rate
  - If O2 desaturation is present –
    - Increase EPAP
    - Increase PS or rate
    - Add O2

BiPAP with AVAPS

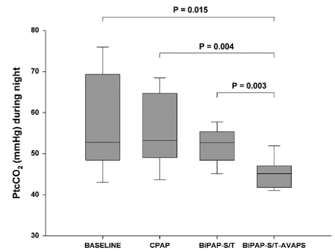
Table 1 Clinical studies on target volume during pressure-preset ventilation

Study	Year	Design	Cohort	Target volume setting	Main target volume outcomes*
Storre *et al*[7] †	2006	6-week cross-over RCT (n=10)	OHS‡	7 ml/kg IBW (n=5), 10 ml/kg IBW (n=5)	► Greater reduction in nocturnal $PtcCO_2$ ► Comparable effect on polysomnography ► Comparable effect on quality of life
Janssens *et al*[10] †	2009	1-day cross-over RCT (n=12)	OHS¶	7.5±0.8 ml/kg body weight	► Greater reduction in nocturnal $PtcCO_2$ ► Worse polysomnography
Ambrogio *et al*[11] †	2009	1-day cross-over RCT (n=28)	Mixed¶	8 ml/kg IBW or 110% of baseline VT	► Comparable effect on polysomnography ► Greater nocturnal minute volume
Crisafulli *et al*[12] †	2009	5-day cross-over RCT (n=9)	COPD‡	8 ml/kg IBW	► Comparable improvements in morning $PaCO_2$ ► Subjective improvement in sleep efficiency
Oscroft *et al*[13] §	2010	8-week cross-over RCT (n=24)	COPD¶	11.0±3.9 l/min (minute volume)	► Comparable effects on: – Daytime blood gases – Lung function and exercise capacity – Quality of life – Nocturnal $PtcCO_2$
Murphy *et al*[14] †	2012	3-month RCT (n=46)	OHS‡	Individual adjustments aimed at achieving control of nocturnal hypoventilation while abolishing obstructive events	► Comparable effects on: – Daytime $PaCO_2$ improvements – Quality of life – Weight loss – Comparable improvements in ESS

Windisch and Storre. Thorax 2012

BiPAP with AVAPS

10 patients with OHS, failed CPAP



Storre JH et al. CHEST 2006

Father and Son: The ASV Song

It's not time to make a change
Just relax, take it easy
It's still early, it's not your fault
There's so much you have to know
Find a chair, settle down
If you want, you can sip your coffee
Look it's ASV, it's new and it's working

I was once like you are now, and I know that it's not easy
To be calm when you've found apneas' going on
But take you time, think a lot
Why, think of everything the patient's got
For he'll be here tomorrow, but his apneas might not

How can I try to relax, when I do, apneas reappear again
It's always been the same, same old story
From the moment the study started, they were supposed to go away
Now, there's a way, and I know that I have to let them stay
I know, I have to let apneas stay

All the times that I have tried, taking all the things I've learned aside
It's hard, but it's harder to ignore them
If ASV's right, I'd agree, but it's them they work, not me
Now, there's a way and I know that I have to let them stay
I know, I have to let apneas stay.