Patient characteristics by group (PAP with and without supplementary O_2)

Table S1. Patient's characteristics by O_2 supplementation to PAP therapy.

	PAP alone (n=125)	**PAP + O_2 (n=100)**	**P value**
Age (years)	57 (44-63)	67 (62-73)	<0.001
Gender, male (%)	78 (62 %)	31 (31%)	0.001
BMI (kg/m^2)	45 (40-50)	41 (38-49)	0.1
Smoking status			
Current smokers, *n* (%)	24 (19%)	13 (13%)	0.06
Comorbidities			
Diabetes mellitus, *n* (%)	30 (24%)	44 (44%)	0.03
Hypertension, *n* (%)	63 (50%)	75 (75%)	0.007
Dyslipidaemia, *n* (%)	50 (40%)	27 (27%)	0.13
Ischemic heart disease, *n* (%)	12 (10%)	14 (14%)	0.67
Atrial Fibrillation, *n* (%)	2 (1.6%)	15 (15%)	0.006
Compensated heart failure, *n* (%)	7 (6%)	24 (24%)	0.005
Stroke, *n* (%)	0	11 (11%)	0.005
Hypothyroidism	19 (15%)	16 (16%)	0.5
ABGs			
pH	7.39 ± 0.03	7.39 ± 0.04	0.45
$PaCO_2$ (mmHg)	47 (46-49)	53 (51-59)	<0.001
PaO_2 (mmHg)	68.8 ± 9.9	59.6 ± 10.9	<0.001
HCO_3^- (mmol/L)	28.7 ± 2.5	33.2 ± 4.3	<0.001
Diagnostic PSG			
AHI	66 (37-89)	47 (31-77)	0.04
REM AHI	71.7 ± 27.9	65.5 ± 24.9	0.24
4% ODI	72.9 ± 31.3	65.4 ± 26.0	0.16
Mean SpO_2 (%)	88 (84-90)	85 (80-87)	<0.001
Minimum SpO_2 (%)	66.8 ± 9.4	63.5 ± 10.5	0.06
TST90 (min)	149 (78-242)	151 (121-241)	0.3
$PtcCO_2$ awake, mmHg	47 (46-49)	54 (51-62)	<0.001
Mean $PtcCO_2$ asleep, mmHg	60.3 ± 5.9	72.6 ± 8.3	<0.001

Data are presented as mean values ± SD or median (25th-75th percentile), unless otherwise indicated.

BMI = Body mass index, ABGs = Arterial blood gases, PSG = Polysomnography, AHI = Apnea-hypopnea index, ODI = oxygen desaturation index, TST90 = total sleep time spent with SpO2 <90%, $PtcCO_2$ = Transcutaneous CO_2.

Analysis in the subgroup of patients that never smoked

Table S2. Comparison of arterial blood gases and questionnaire scores at baseline and at the end of the follow-up period for never smokers (n=142).

	Baseline	End of follow up period	Difference	P value
$PaCO_2$	50.3 (47.2-56.5)	43.0 (39.2-45.0)	-8.8 (-15.2, -5.5)	<0.001
PaO_2	61.5 ±9.1	73.2 ±10.1	11.7 ± 12.1	<0.001
HCO_3^-	32.2 ± 4.4	27.8 ± 3.1	-4.4 ± 5.0	<0.001
ESS	14 (11-16)	7 (4-9)	-7 (-9, -4)	<0.001
BDI	16.6 ± 7.1	9.8 ± 4.9	-6.8 ± 5.3	<0.001
SF-36	73 (67-76)	82 (78-86)	9 (7-12)	<0.001

ESS = Epworth sleepiness scale, BDI= Beck depression inventory, SF-36 = Short form-36.

Effect of PAP therapy in Arterial blood gases and questionnaires scores in the 3 OHS groups

In all three OHS groups separately, the comparison of pretreatment with the last posttreatment measurements demonstrated significant improvements in median $PaCO_2$ values [mild: 47 (46-49) mmHg vs 41.6 (39-44) mmHg, $p < 0.001$; moderate: 53 (51-53) mmHg vs 43.4 (42.5-45.5) mmHg, $p < 0.001$; severe: 61 (58-67) mmHg vs 44 (41-46) mmHg, $p < 0.001$], mean PaO_2 values (mild: 67.6 ± 7.3 mmHg vs 74.7 ± 7.9 mmHg, $p = 0.001$; moderate: 61.3 ± 4.7 mmHg vs 71.6 ± 10.7 mmHg, $p=0.03$; severe: 56.3 ± 9.5 mmHg vs 69.9 ± 10.6 mmHg, $p=0.001$) and mean HCO_3 values (mild: 28.9 ± 1.5 mmHg vs 27.2 ± 3.4 mmHg, $p = 0.007$; moderate: 31.3 ± 3.6 mmHg vs 27.4 ± 3.2 mmHg, $p=0.001$; severe: 36.4 ± 4.5 mmHg vs 28.3 ± 3.1 mmHg, $p<0.001$). $PaCO_2$, PaO_2 and HCO_3^-

measured after follow up were not significantly different between the 3 groups (p=0.075, p=0.27 and 0.57, respectively).

In mild OHS, the ESS changed from 14 (10-17) at baseline to 6 (4-8) after follow up ($p < 0.001$), the BDI from 14.3 ± 7 to 7.9 ± 4.9 ($p < 0.001$) and the SF-36 from 76 (71-81) to 84 (81-89) ($p < 0.001$). In moderate OHS, the ESS changed from 14 912-16) at baseline to 7 (5-9) after follow up ($p < 0.001$), the BDI from 17.4 ± 7.5 to 9.8 ± 5.1 ($p < 0.001$) and the SF-36 from 71 (60-76) to 84 (81-89) ($p<0.001$). In severe OHS, the ESS changed from 13 (10-16) at baseline to 7 (3-9) after follow up (<0.001), the BDI from 16.3 ± 8.1 to 9.6 ± 4.9 ($p < 0.001$) and the SF-36 from 71 (62-75) to 79 (75-87) ($p < 0.001$).

Correlations (Table S3 and S4)

Change in $PaCO_2$ was correlated with hours/day PAP use (r=-0.66, p<0.001), baseline $PaCO_2$ (r=-0.7, p<0.001), PaO_2 (r=0.45, p<0001), HCO_3^- (r=-0.45, p<0.001), $PtcCO_2$ asleep (r=-0.55, p<0.001), $PtcCO_2$ awake (r=-0.67, p<0.001), moderate to severe OHS (r=-0.55, p<0.001) and type of positive airway pressure therapy (Bi-level PAP) (r=-0.29, p=0.014). The use of nocturnal oxygen and total duration of therapy had no impact on the change in $PaCO_2$. In stepwise multiple linear regression models, the magnitude of change in $PaCO_2$ was still associated only with PAP use [β= -1.5 (95% CI, -2.5, -0.5); p=0.007] and baseline $PaCO_2$ [β=-0.87(95 CI%, -1.2, -0.5); p<0.001] after controlling for the potential confounders that were found to be significant.

The change in PaO_2 was related to hours of PAP use (r=0.44, p<0.001), baseline $PaCO_2$ (r=0.28, p=0.02) and baseline PaO_2 (r=-0.6, p<0.001) and after multiple regression only with baseline PaO_2 [β=-0.89 (95% CI -1.2, -0.57); p<0.001]. Change in HCO_3^- was

correlated with hours of PAP use (r=-0.37, p=0.003), baseline $PaCO_2$ (r=-0.52, p<0.001), baseline PaO_2 (r=0.4 p=0.001), baseline HCO_3^- (r=-0.59, p<0.001), overnight mean SaO2 (r=0.3, p=0.015), $PtcCO_2$ asleep (r=-0.42, p=0.011) and $PtcCO_2$ awake (r=-0.5, p=0.002) and moderate to severe OHS group (r=-0.4, p=0.001). In stepwise multiple linear regression models, the magnitude of HCO_3^- change was still associated only with baseline HCO_3^- [β= -0.77, (95% CI -1.1, -0.5); p<0.001).

Change in ESS was correlated with hours of PAP use (r=-0.2, p=0.03) and baseline ESS (r=-0.8, p<0.001), but only with baseline ESS after multiple regression analysis [β=-0.78, (95%CI -0.89, -0.67); p<0.001]. Change in BDI was associated with female gender (r=-0.23, p=0.01), age (r=-0.19, p=0.04), baseline BDI (r=-0.71, p<0.001), baseline SF-36 (r=0.38, p<0.001), presence of heart failure (r=-0.24, p=0.009), $PtcCO_2$ asleep (r=-0.29, p=0.023) and $PtcCO_2$ awake (r=-0.37, p=0.003) and type of positive airway pressure (Bi-level PAP) (r=-0.28, p=0.002). In stepwise multiple linear regression models, the magnitude of change in BDI was still associated with baseline BDI [β=-0.68, (95% CI -0.8, -0.6); p<0.001], baseline SF-36 [β=-0.16, (95% CI -0.25, -0.01); p=0.004), and $PtcCO_2$ awake [β=-0.097, (95% CI -0.26, -0.03); p=0.041].

Change in SF-36 was correlated with hours of PAP use (r=0.39, p<0.001), age (r=0.24, p=0.008), baseline $PaCO_2$ (r=0.2, p=0.03), baseline PaO2 (r=-0.3, p=0.001), nighttime SpO_2_mean (r=-0.22, p=0.013), baseline SF-36 (r=-0.53, p<0.001), $PtcCO_2$ awake (r=0.27, p=0.033), smoking (r=-0.19, p=0.04), diabetes (r=0.2, p=0.021), hypertension (r=0.19, p=0.03), CHD (r=0.19, p=0.03), heart failure (r=0.21, p=0.019) and moderate to severe OHS (r=0.2, p=0.03) . In stepwise multiple linear regression models,

the magnitude of change in SF-36 was still associated with PAP use [β=0.8; (95% CI 0.12, 1.45,); p=0.007] and baseline SF-36 [β=-0.27, (95% CI -0.45, -0.16); p<0.001].

Table S3. Correlation of parameters with change in arterial blood gases.

Parameters	**Change in $PaCO_2$**		**Change in PaO_2**		**Change in HCO_3^-**	
	r Value	**P Value**	**r Value**	**P Value**	**r Value**	**P Value**
Age	-0.12	0.35	-0.02	0.87	-0.14	0.27
Gender, male	-0.062	0.62	0.07	0.60	-0.19	0.41
BMI	-0.1	0.44	0.10	0.45	-0.12	0.34
Smoking	0.1	0.40	-0.21	0.09	0.14	0.27
Diabetes mellitus	-0.07	0.56	0.06	0.63	-0.11	0.40
Hypertension	0.04	0.78	0.005	0.97	0.08	0.55
Ischemic heart disease	-0.11	0.37	0.09	0.46	-0.05	0.68
Atrial Fibrillation	-0.04	0.74	-0.08	0.51	-0.09	0.48
Compensated heart failure	-0.14	0.28	-0.002	0.99	-0.12	0.37
Stroke	-0.001	0.98	-0.04	0.74	-0.19	0.15
$PaCO_2$ (mmHg)	-0.7	<0.001	0.28	0.02	-0.52	<0.001
PaO_2 (mmHg)	0.45	<0.001	-0.6	<0.001	0.40	0.001
HCO_3^-(mmol/L)	-0.45	<0.001	0.24	0.06	-0.59	<0.001
AHI	0.11	0.39	0.05	0.70	0.05	0.70
4% ODI	0.08	0.55	-0.03	0.80	-0.012	0.93
Mean SpO_2 (%)	0.19	0.13	-0.1	0.41	0.31	0.015
Minimum SpO_2 (%)	0.06	0.63	-0.17	0.17	0.19	0.13
TST90 (min)	-0.14	0.33	-0.003	0.98	-0.13	0.39
$PtcCO_2$ awake, mmHg	-0.67	<0.001	0.27	0.11	-0.50	0.002
Mean $PtcCO_2$ asleep, mmHg	-0.55	<0.001	0.26	0.12	-0.42	0.011
PAP, hours/night	-0.66	<0.001	0.44	<0.001	-0.37	0.003

BMI = Body mass index, AHI = Apnea-hypopnea index, ODI = oxygen desaturation index, TST90 = total sleep time spent with SpO2 <90%, $PtcCO_2$ = Transcutaneous CO_2.

Table S4. Correlation of parameters with change in Questionnaire scores.

Parameters	Change in ESS		Change in BDI		Change in SF-36	
	r Value	P Value	r Value	P Value	r Value	P Value
Age	0.05	0.58	-0.19	0.04	0.24	0.008
Gender, male	0.05	0.61	-0.23	0.01	0.13	0.14
BMI	-0.03	0.78	-0.09	0.29	-0.07	0.43
Smoking	0.09	0.36	0.07	0.42	-0.19	0.04
Diabetes mellitus	-0.04	0.67	-0.16	0.07	0.21	0.021
Hypertension	0.05	0.62	-0.13	0.17	0.19	0.03
Ischemic heart disease	0.02	0.86	-0.16	0.08	0.19	0.03
Atrial Fibrillation	0.08	0.39	-0.08	0.41	-0.09	0.48
Compensated heart failure	0.05	0.59	-0.24	0.009	0.21	0.019
Stroke	0.13	0.17	-0.06	0.53	0.03	0.79
$PaCO_2$ (mmHg)	0.12	0.19	-0.14	0.14	0.20	0.03
PaO_2 (mmHg)	0.07	0.49	0.12	0.22	-0.30	0.001
HCO_3^-(mmol/L)	0.03	0.80	-0.09	0.32	0.11	0.23
AHI	-0.16	0.09	0.05	0.56	-0.12	0.21
4% ODI	-0.09	0.32	0.07	0.42	-0.13	0.15
Mean SpO_2 (%)	0.12	0.21	0.06	0.50	-0.22	0.013
Minimum SpO_2 (%)	0.15	0.12	0.04	0.69	-0.11	0.24
TST90 (min)	-0.05	0.61	-0.02	0.83	-0.10	0.34
$PtcCO_2$ awake, mmHg	0.005	0.97	-0.37	0.003	0.27	0.033
Mean $PtcCO_2$ asleep, mmHg	0.03	0.83	-0.29	0.023	0.18	0.17
PAP, hours/night	-0.2	0.03	-0.12	0.18	0.39	<0.001
ESS, baseline	-0.82	<0.001	-0.08	0.37	0.07	0.47
BDI, baseline	0.02	0.80	-0.71	<0.001	0.15	0.09
SF-36, baseline	-0.07	0.49	0.38	<0.001	-0.53	<0.001

BMI = Body mass index, AHI = Apnea-hypopnea index, ODI = oxygen desaturation index, TST90 = total sleep time spent with SpO2 <90%, $PtcCO_2$ = Transcutaneous CO_2, ESS = Epworth sleepiness scale, BDI= Beck depression inventory, SF-36 = Short form-36.

Subgroup analysis by hours of PAP use

Table S5: Comparison of baseline demographics, spirometric measurements and ABG analysis results between patients with PAP use ≥ 6 and < 6 hours of PAP use per night.

Characteristics	<6 hours of PAP use N=97	≥6 hours of PAP use N=128	P-value
Age (years)	61 (48-69)	64 (49-70)	0.55
Gender, male (%)	51 (53%)	57 (44%)	0.34
BMI (kg/m^2)	44 (37-49)	43 (39-50)	0.34
Neck circumference (cm)	45.1 ± 4.2	45.3 ± 4.2	0.80
Waist circumference (cm)	128 (122-141)	134 (124-147)	0.09
Smoking status			
Current smokers	22 (23%)	14 (11%)	0.22
Comorbidities			
Diabetes mellitus, *n* (%)	33 (34%)	42 (33%)	0.89
Hypertension, *n* (%)	54 (55%)	84 (66%)	0.22
Dyslipidaemia, *n* (%)	42 (44%)	38 (30%)	0.16
Ischemic heart disease, *n* (%)	11 (11%)	15 (12%)	0.98
Compensated heart failure	14 (15%)	16 (12%)	0.72
Atrial Fibrillation	7 (8%)	9 (7%)	0.94
Stroke, *n* (%)	4 (4.3%)	7 (6%)	0.64
Hypothyroidism	10 (11%)	24 (19%)	0.27
PFT			
FEV_1, % predicted	85.6 ± 13.3	81.4 ± 10.9	0.33
FVC, % predicted	83.3 ± 10.4	85.6 ± 12.7	0.69
FEV_1/FVC	80 (79.9-86.4)	81 (76-83)	0.45
ABG			
pH	7.39 ± 0.04	7.39 ± 0.03	0.95
PaCO2 (mmHg)	49 (46-53)	51 (47-56)	0.19
PaO2 (mmHg)	67.1 ± 12.9	62.6 ± 9.6	0.05
HCO_3^- (mmol/L)	30.0 ± 3.2	31.3 ± 4.6	0.09

Data are presented as mean values ± SD or median (25th-75th percentile), unless otherwise indicated.

BMI = Body mass index, PFT = Pulmonary function test, FVC = Forced Vital Capacity, FEV_1 = Forced Expiratory Volume in One Second, ABG = Arterial blood gases.

Table S6. Comparison of baseline PSG data and questionnaires scores between patients with PAP use ≥ 6 and < 6 hours of PAP use per night.

	<6 hours of PAP use N=97	≥6 hours of PAP use N=128	P-value
Diagnostic PSG			
AHI	58 (37-87)	57 (35-85)	0.46
AHI REM	67 ± 25	70 ± 28	0.59
AI	50 ± 17	53 ± 23	0.43
4% ODI	71 ± 27	68 ± 31	0.62
Mean SpO_2 (%)	87 (83-90)	86 (80-89)	0.21
Minimum SaO_2 (%)	66 ± 11.	65 ± 9	0.38
TST90 (min)	143 (90-242)	156 (119-241)	0.17
$PtcCO_2$ wake, mmHg	50 (48-52)	53 (47-60)	0.15
$PtcCO_2$ asleep, mmHg	67.1 ± 9.1	67.9 ± 9.9	0.96
After PAP titration			
AHI	4 (3-4)	4 (3-4)	0.43
AI	6.9 ± 2.3	7.4 ± 2.5	0.21
4% ODI	4.6 ± 1.9	4.9 ± 1.6	0.32
Mean SpO_2 (%)	95 (94-95)	95 (94-95)	0.29
Lowest SpO_2 (%)	89.1 ± 1.6	88.3 ± 2.3	0.02
TST90 (min)	1.6 ± 2.1	2.1 ± 2.5	0.34
Questionnaires			
ESS	12 (10-16)	14 (11-16)	0.57
BDI	15.9 ± 6.9	15.1 ± 7.6	0.59
SF-36	74 (67-78)	75 (68-81)	0.50

Data are presented as mean values ± SD or median (25th-75th percentile), unless otherwise indicated.

PSG = Polysomnography, AHI = Apnoea-hypopnea index, AI = Arousal index, ODI = oxygen desaturation index, TST90 = total sleep time spent with SpO2 <90%, $PtcCO_2$ =

Transcutaneous CO_2, PAP = Positive airway pressure, ESS = Epworth sleepiness scale, BDI= Beck depression inventory, SF-36 = Short form-36.

Table S7. Comparisons of changes in arterial blood gases and questionnaire scores over the follow up according hours of PAP use per night in never smokers.

	<6 hours of PAP use	**≥6 hours of PAP use**	**P-value**
	All Patients		
	(n=55)	**(n=87)**	
$PaCO_2$	-3.0 (-5.6, -2.5)	-10.7 (-16.6, -8.2)	<0.001
PaO_2	4.9 ± 8.1	14.4 ± 12.4	0.015
HCO_3^-	-1.5 ± 2.2	-5.6 ± 5.4	0.01
ESS	-6 (-10, -3)	-7 (-9, -5)	0.51
BDI	-6.5 ± 4.6	-7.0 ± 5.8	0.73
SF-36	8 (3-10)	11 (8-14)	0.002

Data are presented as mean values ± SD or median (25th-75th percentile)
ESS = Epworth sleepiness scale, BDI= Beck depression inventory, SF-36 = Short form-36.

Table S8. Comparisons of changes in arterial blood gases and questionnaire scores over the follow up according hours of PAP use per night.

	<4 hours of PAP use	4-5.9 hours of PAP use	6-7 hours of PAP use	>7 hours of PAP use	P-Value Across all
	Group 1 (n=27)	Group 2 (n=69)	Group 3 (n=82)	Group 4 (n=47)	
$PaCO_2$	-2.7 (-3.1, -2.1)	-4.7 (-6.4, -2.7)	-9.6 (-15.0, -7.4)$^{\#**}$	-13 (-17.9, -8.2)$^{\$\&}$	<0.001
PaO_2	-14.1 ± 20.0	4.1 ± 9.3*	13.4 ± 13.2$^{\#}$	13.6 ± 11.0$^{\$}$	<0.001
HCO_3^-	-0.5 ± 3.4	-1.3 ± 2.2	-5.6 ± 6.0**	-4.6 ± 6.1	0.012
ESS	-6 (-11, -3)	-5 (-9, -2)	-6 (-9, -3)	-9 (-12, -6)	0.15
BDI	-5.7 ± 3.3	-6.3 ± 4.4	-6.8 ± 5.9	-7.6 ± 7.1	0.71
SF-36	7 (5-8)	7.5 (4-11)	8 (7-11)$^{\#}$	11 (8-16)$^{\$\&¥}$	0.001

Data are presented as mean values ± SD or median (25th-75th percentile).

ESS = Epworth sleepiness scale, BDI= Beck depression inventory, SF-36 = Short form-36.

# P < 0.05 Group 3 vs 1 OHS; *P < 0.05 Group 2 vs 1 OHS; **P < 0.05 Group 3 vs 2, $P<0.05 Group 4 vs 1, & P<0.05 Group 4 vs 2, ¥ Group 4 vs 3.