Online supplement

Table S1. Details for the 9 clinical studies included

Short name	**ADISAS**	**AGIRSAS ADOM**	**BPCO**	**BPCO-SAS**	**DIAMETASAS**	**Aortic Dissection**	**INFRASAS**	**VALSAS**	**NIV-OHS**
Clinical trial number	NCT01196845	NCT01090297	NCT00404430	NCT01195064	NA	NCT01068691	NCT01089257	NCT00409487	NCT00603096
Ethics committee* approval date	07/10/2009	29/07/2009	10/01/2007	16/10/2009	02/08/2006	06/02/2008	04/07/2007	07/06/2006	10/05/2006
Design	RCT	RCT	Observational study	Observational study	RCT	RCT	Observational study	RCT	RCT
Primary outcome	Inflammation in adipose tissue	Clinical blood pressure	Peripheral arterial tone	Peripheral arterial tone	Flow-deviated vasodilatation	Ambulatory blood pressure monitoring	Anatomic and functional vascular study	Ambulatory blood pressure monitoring	Diurnal $PaCO_2$
Key eligibility criteria	OSA patients obese or not who need CPAP treatment	OSA patients who need CPAP treatment	Patients with exacerbated COPD	Patient suspected for OSA or BPCO with planned coronary artery bypass graft surgery or vascular surgery	Patients with metabolic syndrome	Patients suspected for OSA or BPCO and surgically treated for type A acute aortic syndrome	Patients suspected for OSA	OSA patients with hyperten-sion	Patients with obesity-hypoventi-lation syndrome
Referral base	24	322	102	58	37	156	95	28	160
Publications (reference)		1	2 to 5	5		6	7	8	9,10

* Ethics committee: Comité de Protection des Personnes- Sud Est V IRB0006705
NA, not applicable since confidential trial; RCT, randomized controlled trial

Table S2. Patients' characteristics for the 9 clinical studies included

Short name	ADISAS	AGIRSAS ADOM	BPCO	BPCO-SAS	DIAMETASAS	Aortic dissection	INFRASAS	VALSAS	NIV-OHS
Number of patients*	22	313	99	53	34	131	90	28	123
Male (n (%))	22 (100)	221 (70.6)	81 (81.8)	43 (86)	18 (52.9)	113 (86.3)	74 (82.2)	22 (78.6)	50 (40.7)
Age (yrs)	54.4 (8.1)	57.4 (11.1)	63.7 (8.5)	62.7 (9.1)	59.4 (6.9)	49.1 (10.3)	52 (10.7)	56.4 (8.5)	53.2 (12.7)
BMI (kg/m^2)	31.2 (8.2)	31 (6.6)	25.4 (4.7)	26.3 (4)	29.5 (3.4)	26.6 (3.3)	25.2 (2.8)	28.9 (4.9)	39.3 (5.5)
Normal (n (%))	5 (22.7)	41 (13.1)	60 (60.6)	23 (43.4)	1 (2.9)	40 (30.5)	40 (44.4)	5 (17.9)	-
Overweight (n (%))	6 (27.3)	117 (37.4)	44 (44.4)	22 (41.5)	18 (52.9)	77 (58.8)	49 (54.4)	14 (50)	2 (1.6)
Obese (n (%))	5 (22.7)	86 (27.5)	40 (40.4)	6 (11.3)	12 (35.3)	12 (9.2)	1 (1.1)	5 (17.9)	24 (19.5)
Severely obese (n (%))	4 (18.2)	44 (14.1)	12 (12.1)	2 (3.8)	3 (8.8)	1 (0.8)	-	4 (14.3)	45 (36.6)
Morbidly obese (n (%))	2 (9.1)	25 (8)	3 (3)	-	-	1 (0.8)	-	-	52 (42.3)
Hypertension (n (%))	12 (54.5)	268 (85.6)	45 (45.5)	45 (84.9)	32 (94.1)	111 (84.7)	62 (68.9)	28 (100)	76 (61.8)
Diabetes (n (%))	6 (27.3)	175 (55.9)	37 (37.4)	29 (54.7)	24 (70.6)	24 (18.3)	15 (16.7)	12 (42.9)	71 (57.7)
Dyslipidemia (n (%))	18 (81.8)	207 (66.1)	56 (.)	48 (90.6)	29 (85.3)	81 (61.8)	42 (46.7)	15 (53.6)	74 (60.2)
OSA (n (%))	17 (100)	304 (97.1)	28 (65.1)	27 (56.3)	20 (58.8)	131 (100)	56 (62.2)	23 (82.1)	77 (68.8)
SBP (mmHg)	130.1 ± 11.3	134 ± 14.1	136.8 ± 16.8	132.9 ± 16.2	147 ± 17.3	131.6 ± 16.5	121.1 ± 13.8	153.2 ± 14.8	130.3 ± 16.9)
DBP (mmHg)	79.7 ± 9.4	82.5 ± 9	77 ± 9.8	71.7 ± 11.6	89.6 ± 14	86.2 ± 10.1	74.7 ± 11.3	100.2 ± 11.4	73.8 ± 12.1)
HR (bpm)	64.8 ± 13	75.5 ± 10.7	68.8 ± 13.2	65.7 ± 11.2	66.9 ± 12.2	64.4 ± 9.8	58.2 ± 8.3	68.9 ± 12.6	-
PWV (m/s)	10.2 ± 1.6	10.7 ± 2.2	12 ± 2.4	11.6 ± 2.7	10.4 ± 1.4	9.1 ± 1.5	9.6 ± 1.6	10.5 ± 2.3	9.7 ± 2.4
AHI (events/h)	44.9 ± 21.2	42.8 ± 21	30.1 ± 30.4	24.7 ± 23.6	22.2 ± 22.3	40.6 ± 16	23.8 ± 19.6	30.9 ± 17.8	38.3 ± 33.4
Mean nocturnal SaO_2 (%)	92.7 ± 2.4	92.9 ± 2.9	91.7 ± 2.1	93.1 ± 2	92.9 ± 1.8	93.4 ± 2	94.1 ± 1.9	93.3 ± 2.3	92 ± 3.6
SaO_2 < 90% (%)	7 ± 13.7	13.2 ± 19.5	14.8 ± 21.7	7.2 ± 14.4	4.3 ± 5.4	6.2 ± 12.8	4.2 ± 10.3	11 ± 22.4	16.8 ± 23.3
ESS score	10.3 ± 5.3	10 ± 5.3	-	5.6 ± 3.7	7.7 ± 5.2	10 ± 5.3	8.9 ± 5.1	9.9 ± 4	10.1 ± 4.8

Results are expressed as mean ± SD or n (%). The percentages correspond to patients with missing data before imputation. *Number of patients from the referral base (Table S1) after exclusion of patients without PWV data.
AHI, apnea-hypopnea index; BMI, body mass index; DBP, diastolic blood pressure; ESS, Epworth Sleepiness Scale; SaO_2, oxygen saturation; HR, heart rate; PWV, Pulse wave velocity; $SaO_2 < 90\%$, percentage of recording time spent at a $SaO_2 < 90\%$; SBP, systolic blood pressure.

Statistical complement about the data imputation method used

Missing values were imputed using a multiple imputation method when the proportion of missing values was < 20%. Five datasets were generated using logistic regression for qualitative variables or linear regression for quantitative variables, considering that missing values were random. Two regression models were used to impute missing data: a logistic regression model for qualitative (binary) variables and a linear regression method for quantitative variables. To confirm the imputation strategy, a sensitivity analysis was performed by comparing the results based on complete cases and multiple imputation. This comparison showed no difference. Categorical variables were first imputed using a continuous model and then the imputed values were categorized using the same threshold in each dataset. The initial study was introduced as a fixed effect in all regressions models. After imputation, the results of the five dataset were combined using the MI ANALYZE procedure from SAS, which corresponded to the Rubin's rules.

Table S3. Patients' characteristics for the whole population

	Initial dataset N = 893	**Missing N (%)**	**Imputed dataset N = 4465**
Male (n (%))	644 (72)	3 (0.3)	3232 (72)
Age (yrs)	56 ± 11	1 (0.1)	56 ± 11
BMI (kg/m^2)	29.9 ± 6.9	0 (0)	29.9 ± 6.9
Normal (n (%))	199 (22)		995 (22)
Overweight (n (%))	345 (39)		1725 (39)
Obese (n (%))	163 (18)		815 (18)
Severely obese (n (%))	106 (12)		530 (12)
Morbidly obese (n (%))	80 (9)		400 (9)
Hypertension (n (%))	694 (78)	48 (5.4)	3470 (78)
Type 2 diabetes (n (%))	401 (45)	0	2005 (45)
Dyslipidaemia (n (%))	551 (62)	109 (12.2)	2755 (62)
OSA (n (%))	683 (84)	77 (8.6)	3691 (83)
SBP (mmHg)	133 ± 17	47 (5.3)	133 ± 17
DBP (mmHg)	81 ± 12	46 (5.2)	81 ± 12
HR (bpm)	69 ± 12	167 (18.7)	70 ± 13
PWV (m/s)	10.4 ± 2.3	0 (0)	10.4 ± 2.3
AHI (events/h)	36.8 ± 24.1	77 (8.6)	36.1 ± 23.9
Mean nocturnal SaO_2 (%)	92.9 ± 2.7	86 (9.6)	92.8 ± 2.7
SaO_2 < 90% (% of recording time)	10.8 ± 18.3	94 (10.5)	10.7 ± 18.0
ESS score	9.5 ± 5.2	162 (18.1)	9.4 ± 5.1

Results are expressed as mean ± SD or n (%). Percentages of initial data set correspond to patients with missing data before imputation.

AHI, apnoea-hypopnea index; BMI, body mass index; DBP, diastolic blood pressure; ESS, Epworth Sleepiness Scale; SaO_2, oxygen saturation; HR, heart rate; PWV, Pulse wave velocity; $SaO_2 < 90\%$, percentage of recording time spent at a $SaO_2 < 90\%$; SBP, systolic blood pressure.
All comparisons between initial and imputed datasets were not significant.

Statistical complement about the two-step meta-analysis performed

A two-step individual patient data (IPD) meta-analysis was first performed to assess the heterogeneity between studies. The first step consisted of aggregating the individual data and the second step used a DerSimonian and Laird random effects meta-analysis model. The heterogeneity between studies was measured using the I^2 inconsistency index, which provides an estimation of the variability due to the heterogeneity rather than chance. An I^2 index greater than 60% reflects high heterogeneity. Finally, the robustness of the results was assessed using sensitivity analysis by leaving out one study.

The two-step IPD meta-analysis showed that the test for heterogeneity was not significant (I^2=44.7%, p=0.09), which means that only limited heterogeneity was observed across the 9 studies.

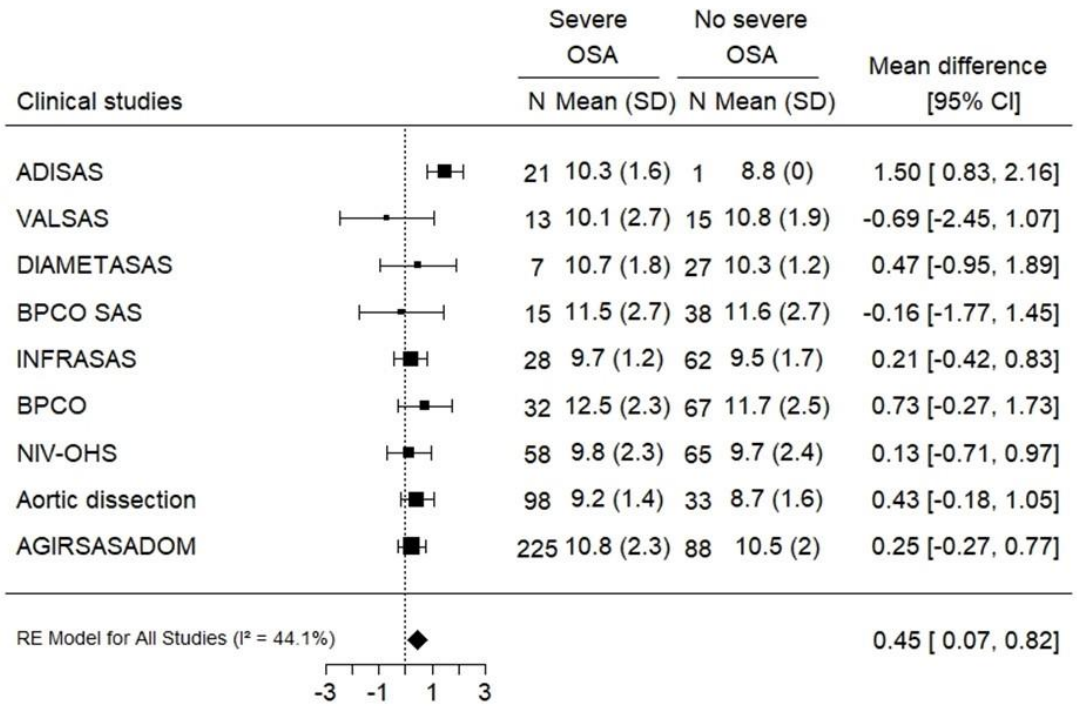
Finally, the result of the two-step meta-analysis showed a slight association between severe OSA and PWV (Figure S1). However, this result should be interpreted carefully because there was no adjustment on the different confounders. Moreover, the leave-one-out study we performed showed that the main heterogeneity was mainly due to one study (ADISAS) (Table S4) and by excluding this study the result was not significant. The observed trend was not significant after adjustment in the one-step meta-analysis.

Table S4. Result of the leave-one-out analysis

Study	Estimate (SE)	P value	I^2
ADISAS	0.2761 (0.1443)	0.0557	0
AGIRSASADOM	0.4794 (0.2266)	0.0344	46.4611
BPCO	0.4097 (0.2130)	0.0544	50.0736
BPCO SAS	0.4739 (0.1993)	0.0174	47.689
DIAMETASAS	0.4405 (0.2053)	0.0319	49.7725
Aortic dissection	0.4380 (0.2285)	0.0553	50.0152
INFRASAS	0.4827 (0.2213)	0.0292	47.2912
VALSAS	0.4923 (0.1939)	0.0111	45.4131
NIV-OHS	0.4838 (0.2129)	0.023	47.9618

The leave-one-out verifies the robustness of the results by leaving out one study at a time.

Figure S1. Forest plot of the influence of the OSA severity on PWV



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