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OSA, metabolic syndrome and CPAP: Effect on cardiac remodeling in subjects with abdominal obesity

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Summary
Background: We evaluated whether obstructive sleep apnoea (OSA) and continuous positive airway pressure (CPAP) treatment influence left ventricular (LV) remodelling independently of abdominal obesity and metabolic syndrome (MetS).
Methods: Cardiorespiratory examination, 24-h BP monitoring and echocardiogram were performed in overweight/obese patients with increased abdominal adiposity and symptoms suggesting OSA : OSA/MetS (n.50), OSA/noMetS (n.22), noOSA/MetS (n.29), noOSA/noMets (n.16). The evaluation was repeated in 41 patients after ≥18 months of CPAP.
Results: Despite similar age, gender, BMI and 24-h BP, the 2 groups with MetS had greater LV remodelling (LV hypertrophy and diastolic dysfunction) than the 2 groups without MetS. From multiple regression analysis independent determinants for LV mass were MetS, 24-h systolic BP and age, for LV diastolic function were LV mass index, MetS and age. After CPAP, the 20 patients with decreased body weight showed diastolic BP decrease, LV hypertrophy regression and diastolic function improvement, whereas, despite similar respiratory improvement, BP and LV parameters were unchanged in the 21 patients with body weight unchanged/increased.

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Conclusion: In patients with increased abdominal adiposity, LV remodelling is not associated to OSA per se; chronic CPAP treatment does not influence LV remodelling whose regression is mainly linked to body weight decrease.

Introduction

Obstructive sleep apnoea (OSA) is associated with increased cardiovascular morbidity and mortality.[1] This high cardiovascular risk is accounted for by factors linked to OSA per se, including its mechanical, neurohumoral, inflammatory and oxidative effects, and by cardiovascular risk factors, such as male gender and visceral obesity, that are also risk factors for OSA, making it difficult to distinguish the possible independent role of OSA.[1] A relevant role in increasing cardiovascular risk is probably played by the development of left ventricular (LV) remodelling: in fact OSA has been associated to LV morpho-functional changes, mainly characterized by myocardial hypertrophy and diastolic dysfunction, both known independent cardiovascular risk factors.[2,3] Actually the studies about LV remodelling in OSA reached partly different conclusions about characteristics and extent of LV changes and also about the possible direct role of OSA as a cause of LV remodelling.[4–8] As well, few data are available about the effects of continuous positive airway pressure (CPAP), the standard therapy for OSA,[9] on LV characteristics: a $\leq$6-month treatment with CPAP appears to induce at least some degree of regression of myocardial hypertrophy and/or diastolic dysfunction.[6,7,10,11]

The different conclusions reached by studies on LV remodelling in OSA might be accounted for by differences with regard to methods employed, LV parameters evaluated and patients characteristics, such as body weight and blood pressure (BP). In fact, visceral obesity and arterial hypertension are highly prevalent in OSA and both are linked per se to the development of LV hypertrophy and diastolic dysfunction.[12] Moreover, all the studies about LV morphology and function in OSA did not investigate the presence of metabolic syndrome (MetS). This cluster of cardiovascular risk factors, including visceral obesity, high BP, fasting hyperglycaemia and atherosclerotic dyslipidemia,[13] has been linked per se to the development of LV remodelling in the general population and in hypertensive subjects.[14,15] MetS prevalence seems to be high in OSA, either due to the concomitant abdominal obesity or to a direct link between OSA and MetS.[16–18]

Moving from these considerations, we evaluated, in subjects with increased visceral adiposity, whether OSA and CPAP treatment influence LV remodelling independently of coexisting abdominal obesity and MetS. To this goal we designed a study divided into 2 parts : 1) a cross-sectional part aimed to examine the association between OSA, MetS and LV characteristics, 2) a longitudinal part aimed to evaluate the effects of chronic ($\geq$18 months) CPAP treatment on LV morphology and function, taking also into account the concomitant changes in body weight, because of the known influence of weight changes on LV morpho-functional characteristics in obesity.[19]

Methods

Patients and design

Cross-sectional study

Among the subjects referred to the respiratory outpatients' clinics of Cuasso al Monte and Somma Lombardo Hospitals for symptoms suggesting possible OSA (i.e. daytime hypersomnolence and/or snoring) we consecutively enrolled patients with the following characteristics: BMI $>$25 kg/m^2 and waist circumference $>$88 cm in women, $>$102 cm in men, LV echocardiogram of good quality and repeatable, no previous or current treatment with statins, beta-blockers or diuretics, no diabetes mellitus, COPD or thyroid disorders, no clinical, electrocardiographic or echocardiographic signs of heart failure, coronary artery disease or valvular heart diseases, no history of cerebrovascular or peripheral artery disease. We also excluded the patients with upper airway resistance syndrome or central sleep apnoea (Recruitment Flowchart, as Figure S1, online supplement file).

Following these criteria, we enrolled 117 patients (89 men, 28 women, mean age 55 $\pm$ 10 years, mean BMI 31.8 $\pm$ 4.6 kg/m^2, mean waist circumference 110.3 $\pm$ 7.4 cm).

Each patient underwent: daytime sleepiness evaluation with Epworth Sleepiness Scale score,[20] night-time cardio-respiratory examination, 24-h ambulatory BP monitoring, LV echocardiogram, blood tests for the evaluation of metabolic profile.

Longitudinal study

All the patients with OSA underwent counselling about lifestyle corrections (dietary changes and regular physical activity aimed to lose weight). The recommended lifestyle changes and the adherence to them were discussed at any following visit. All the 56 patients with apnoea/hypopnoea index (AHI) $\geq$ 15 events/hour began CPAP treatment and underwent a visit at the respiratory clinic after 6 months and then once a year.

After at least 18 months of CPAP treatment, a second evaluation (Epworth sleepiness scale, night-time cardio-respiratory examination, 24-h ambulatory BP monitoring, LV echocardiogram and blood tests) was performed in 41 patients who have not changed the basal drug treatment and used CPAP $\geq$ 4 h per night. The other 15 patients treated with CPAP were excluded from the second evaluation because of anti-hypertensive treatment changes (7 patients) and/or CPAP use $<$ 4 h per night (10 patients).

The study was approved by the Ethical Committee of the Ospedale di Circolo and all the patients gave their informed consent.

See online supplementary file for: MetS diagnosis, HOMA index evaluation, night-time cardio-respiratory examination,

diagnosis of OSA, CPAP ventilation, 24 h ambulatory BP monitoring, echocardiographic examination.

Statistical analysis

The statistical analysis was performed using the SPSS 11.5 software; data are expressed as mean values (±SD) or percentage; a probability value <0.05 (two-sided) was considered statistically significant.

Cross-sectional study

The patients were divided according to the presence/absence of OSA and MetS : OSA/MetS, OSA/noMetS, noOSA/MetS, noOSA/noMetS. We compared mean values of all the parameters among the 4 groups by means of 2 (between OSA and no OSA) by 2 (between MetS and no MetS) ANOVA, followed by the test of Scheffé. We also compared mean values of all the parameters among patients with mild (AHI 5—14 events/hour), moderate (AHI 15—29 events/hour) and severe OSA (AHI $\geq$ 30 events/hour), using one-way analysis of variance (ANOVA) and Scheffé test. This latter was chosen since it is known to be conservative and reliable in *post-hoc* analysis between three or more groups.[21] Chi-square test was used to compare proportions. Multiple regression analyses were performed to identify independent predictors of LV mass and diastolic function by a stepwise procedure with, respectively, LV mass index and Em/Am ratio as dependent variables. The independent variables were age, gender, BMI, 24-h systolic and diastolic BP, 24-h heart rate, AHI, oxygen desaturation index (ODI), Epworth Sleepiness score and MetS (as a dummy variable by assigning 1 to MetS and 2 to noMetS); LV mass index was added as independent variable in the analysis for Em/Am ratio. Both regression analyses were repeated removing MetS and adding its individual components, with the exclusion of waist circumference because of its high correlation with BMI.

Longitudinal study

By means of paired Student's *t* test we evaluated the changes of respiratory, BP, metabolic and LV parameters from basal to second evaluation in 41 patients treated with CPAP.

Then the patients were divided on the basis of weight changes from baseline : patients with weight decreased ($\geq$2 kg) and patients with weight unchanged or increased ($\geq$2 kg). We used 2 (between decreased weight and unchanged/increased weight group) by 2 (repeated measures with 2 levels : basal and second evaluation) ANOVA, followed by the test of Scheffé, in order 1) to compare basal values between the 2 groups, 2) to evaluate longitudinal changes within each group, 3) to compare the effects of weight changes (decrease vs no change/increase) on respiratory, BP, metabolic and LV parameters.

Results

Cross-sectional study

OSA was diagnosed in 72 patients : 16 mild OSA (AHI 5-14 events/hour), 18 moderate OSA (AHI 15-29 events/hour) and 38 severe OSA (AHI $\geq$ 30 events/hour). MetS was found in 79 patients and its prevalence was similar among subjects with mild, moderate, severe OSA and without OSA (Figure 1).

We divided the patients according to the presence/absence of OSA and MetS : OSA/MetS (50 patients), OSA/noMetS (22 patients), noOSA/MetS (29 patients), noOSA/noMetS (16 patients). The 4 groups were not significantly different with regard to age, gender, BMI, waist circumference, heart rate and BP throughout the 24 h (Table 1 and Table S1, see online supplement file). The prevalence of hypertension (24-h BP $>$ 125 and/or 80 mmHg)[22] and of chronic anti-hypertensive treatment (with ACE inhibitors, Angiotensin II receptors blockers and/or calcium-antagonists) were also similar among the 4 groups (Table 1). AHI, ODI and Epworth Sleepiness score were higher and mean nocturnal O_2 saturation lower in the 2 groups with OSA (Table 1), whereas triglycerides, fasting glucose and HOMA index were higher and HDL cholesterol lower in the 2 groups with MetS (Table S1, see online supplement file).

With regard to LV characteristics (Table 1), LV end-diastolic diameter and LV ejection fraction were normal in all the subjects ($<$57 mm, $\geq$55%)[22] and similar among the 4 groups. Compared to the 2 groups without MetS, the 2 groups with MetS had higher septal and posterior wall thickness, relative wall thickness and LV mass index, lower LV diastolic indices (Em/Am and E′/A′) and greater prevalence of LV hypertrophy (LV mass $>$ 44 g/m$^{2.7}$ in women, $>$48 g/m$^{2.7}$ in men)[23] and diastolic dysfunction (at least 2 of the followings : $E/A < 1$, $E'/A' < 1$, $Em/Am < 1$). No differences in LV morpho-functional parameters were found between the 2 groups with MetS (OSA/MetS and noOSA/MetS), as well as between the 2 groups without MetS (OSA/noMetS and noOSA/noMetS). ANOVA (2×2 factors) showed a significant effect of MetS on metabolic parameters, septal and posterior wall thickness, LV mass index and diastolic parameters, with a significant effect of OSA on respiratory parameters only.

Mean values of LV morpho-functional parameters were not significantly different comparing patients with mild, moderate and severe OSA (data not shown).

From stepwise multiple regression analyses (Table S2), the main independent predictors of LV mass index were MetS, 24-h systolic BP and age; after removing MetS from the equation, the main independent determinants were 24-h systolic BP, BMI and age. The main independent predictors

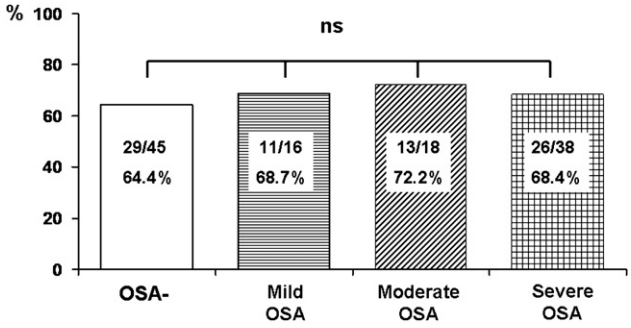

Figure 1 Prevalence of metabolic syndrome in patients with mild, moderate, severe OSA and without OSA (OSA-).

Table 1 Mean values (±SD) of anthropometric, respiratory and LV parameters in patients subdivided on the basis of presence/absence of OSA (OSA, noOSA) and MetS (MetS, noMetS).

Anthropometric parameters	OSA		noOSA		ANOVA	
	MetS ($n = 50$)	noMetS ($n = 22$)	MetS ($n = 29$)	noMetS ($n = 16$)	OSA	MetS
Age, years	55 ± 10	54 ± 12	56 ± 9	56 ± 11	ns	ns
Men/women	40/10	17/5	20/9	12/4	ns	ns
Body mass index, kg/m^2	32.4 ± 4.6	31.9 ± 6.1	31.3 ± 3.8	31.8 ± 4.6	ns	ns
Waist circumference, cm	111.7 ± 8.2	110.5 ± 7.4	108.4 ± 7.6	110.2 ± 6.9	ns	ns
Respiratory parameters						
AHI, events per hour	39.3 ± 24[a]	37.8 ± 21[a]	2.6 ± 1.4	2.7 ± 1.5	<0.001	ns
ODI, events per hour	38.3 ± 25.7[a]	41.5 ± 27.8[a]	4.1 ± 6.1	4.3 ± 3.9	<0.001	ns
Mean nocturnal SaO_2, %	91.2 ± 5.1[a]	90.9 ± 4.6[a]	95.8 ± 1.8	95.5 ± 1.6	<0.001	ns
Epworth Sleepiness score	10.4 ± 5.7[a]	10.7 ± 4.6[a]	5.2 ± 3.4	5.3 ± 3.7	<0.001	ns
LV parameters						
LV diastolic diameter, mm	48.7 ± 6.5	49.3 ± 4.8	48.6 ± 6.7	48.9 ± 4.6	ns	ns
Septal thickness, mm	11.3 ± 1.7[b]	9.7 ± 1.5	11.5 ± 1.5[b]	9.8 ± 1.2	ns	<0.001
Wall thickness, mm	11.1 ± 1.4[b]	9.5 ± 1.5	10.9 ± 1.6[b]	9.5 ± 1.2	ns	<0.001
Relative wall thickness	0.46 ± 0.07[b]	0.39 ± 0.05	0.46 ± 0.08[b]	0.39 ± 0.06	ns	<0.001
LV mass index, g/m$^{2.7}$	58.6 ± 17.6[b]	45.2 ± 12.6	59.5 ± 18.8[b]	47.4 ± 13.4	ns	<0.001
Ejection fraction,%	64 ± 5	62 ± 4	63 ± 7	64 ± 6	ns	ns
E/A	0.94 ± 0.24	0.96 ± 0.22	0.98 ± 0.32	0.97 ± 0.26	ns	ns
Em/Am	0.84 ± 0.27[b]	1.08 ± 0.31	0.87 ± 0.29[b]	1.02 ± 0.33	ns	0.005
E′/A′	0.76 ± 0.25[b]	0.95 ± 0.27	0.73 ± 0.30[b]	0.97 ± 0.24	ns	0.002
LV hypertrophy, n. (%)	42 (84%)[b]	9 (41%)	24 (82.7%)[b]	7 (43.7%)	ns	<0.001
Diastolic dysfunction, n.(%)	30 (60%)[b]	4 (18.2%)	19 (65.5%)[b]	3 (18.7%)	ns	<0.001

AHI: apnoea/hypopnoea index; ODI : oxigen desaturation index; SaO_2 : arterial oxigen saturation; LV: left ventricular; E/A : ratio between peak early (E) and peak late transmitral flow velocity (A); Em/Am: ratio between peak early (Em) and peak late (Am) diastolic velocity of myocardial lateral wall; E′A′ : ratio between peak early (E′) and peak late (A′) diastolic velocity of interventricular septum.
[a] $P < 0.001$ OSA vs no OSA.
[b] $0.02 < P < 0.001$ MetS vs noMetS.

of Em/Am, index of LV diastolic function, were LV mass index, MetS and age; after removing MetS, BMI entered the equation. AHI, ODI, Epworth Sleepiness score and the single components of MetS did not enter the equations.

Longitudinal study

Mean length of CPAP treatment was 23.9 ± 4.8 months. After CPAP treatment the 41 patients showed the following significant changes: decrease of weight, BMI and waist circumference, improvement of all respiratory parameters, reduction of 24-h, daytime and night-time diastolic BP and heart rate, decrease of triglycerides, fasting glycaemia and HOMA index, decrease of relative wall thickness and LV mass index, due to significant reduction of septal and posterior wall thickness, with improvement of LV diastolic parameters (E/A and Em/Am)(Table S3, see online supplement file).

Looking at weight changes during treatment we found that from basal to second evaluation body weight decreased ≥2 kg in 20 patients (↓weight group, from 100.3 ± 17 kg to 93.6 ± 15.4 kg, $P < 0.0001$), whereas in 21 patients body weight was unchanged (12 patients) or increased ≥ 2 kg (9 patients) (=/↑weight group, from 91.8 ± 13.2 kg to 93.9 ± 13.9 kg, $p = 0.015$). At baseline the 2 groups were similar with regard to age (↓weight 55 ± 10 years vs =/↑weight 53 ± 9 years, ns), gender (men/women ↓weight 15/5 vs =/↑weight 18/3, ns), heart rate and BP throughout the 24 h, metabolic parameters and LV systolic and diastolic indices (Tables 2 and 3); ↓weight group had lower height (1.68 ± 0.09 m vs 1.74 ± 0.08 m, $p = 0.03$), higher BMI, waist circumference and LV mass index (Tables 2 and 3). Length of CPAP treatment (↓weight 23.2 ± 4.3 months vs =/↑weight 24.5 ± 5.2 months, ns) and average nightly use of CPAP (↓weight 5.5 ± 1.2 h/night vs =/↑weight 5.7 ± 1 h/night, ns) were similar between the 2 groups. After treatment all respiratory parameters improved significantly in both groups (Table 2); the extent of improvement was similar between the 2 groups: AHI ↓weight −89.3 ± 15.5% vs =/↑weight −88.6 ± 16.8%, ns; ODI ↓weight −93.4 ± 7.6% vs =/↑weight −92.6 ± 10.2%, ns.

The ↓weight group showed the following significant changes: decrease of BMI, waist circumference, diastolic BP and heart rate throughout the 24 h, triglycerides, fasting glucose, HOMA index, relative wall thickness, LV mass index (due to reduction of septal and posterior wall thickness), improvement of LV diastolic indices (Tables 2 and 3). In the group with =/↑weight metabolic, BP and LV parameters remained unchanged (Tables 2 and 3). ANOVA (2x2 factors) showed a significant effect of weight change on BP, heart rate, metabolic and LV parameters, with a significant effect of CPAP treatment only on respiratory parameters (Tables 2 and 3).

Discussion

As far as we know this is the first study that evaluated: 1) LV remodelling in OSA taking into account the presence of

Table 2 Mean (±SD) values of anthropometric, respiratory and BP parameters before and after CPAP in patients with decreased weight (↓weight) and in patients with unchanged/increased weight (=/↑weight).

Anthropometric parameters	↓ weight ($n = 20$)		=/↑ weight ($n = 21$)		ANOVA	
	basal	CPAP	basal	CPAP	CPAP	Weight change
Body mass index, kg/m^2	35.1 ± 4.6[b]	32.9 ± 4.5[c]	30.8 ± 4.1	31.1 ± 4.3[c]	ns	0.002
Waist circumference, cm	115.8 ± 8.9[a]	110.7 ± 9.9[c]	107.3 ± 10.2	107.9 ± 11.1	ns	0.011
Respiratory parameters						
AHI, events per hour	45.6 ± 20.3	4.7 ± 6.1[c]	45.3 ± 22.3	5.3 ± 6.5[c]	<0.001	ns
ODI, events per hour	45 ± 19.5	2.9 ± 3.1[c]	44.4 ± 20.8	3.4 ± 4.2[c]	<0.001	ns
Mean nocturnal SaO_2,%	89.9 ± 6.6	95.5 ± 1.3[c]	90.5 ± 5.3	95.7 ± 1.6[c]	<0.001	ns
Epworth sleepiness scale	12.4 ± 4.4	6.5 ± 3.9[c]	11.3 ± 4.8	4.5 ± 3.3[c]	<0.001	ns
BP and HR parameters						
Systolic BP 24h, mmHg	128 ± 10	125 ± 11	126 ± 12	125 ± 13	ns	ns
Diastolic BP 24h, mmHg	78 ± 10	72 ± 9[c]	77 ± 9	76 ± 11	ns	0.016
Heart rate 24h, bpm	73 ± 9	67 ± 8[c]	73 ± 10	72 ± 11	ns	0.021
Systolic BP day, mmHg	131 ± 10	129 ± 12	129 ± 11	127 ± 14	ns	ns
Diastolic BP day, mmHg	82 ± 10	76 ± 11[c]	81 ± 9	80 ± 12	ns	0.019
Heart rate day, bpm	76 ± 9	72 ± 9[c]	78 ± 10	76 ± 12	ns	0.015
Systolic BP night, mmHg	121 ± 12	116 ± 13	117 ± 11	117 ± 14	ns	ns
Diastolic BP night, mmHg	71 ± 10	65 ± 8[c]	71 ± 10	70 ± 11	ns	0.013
Heart rate night, bpm	69 ± 9	60 ± 8[c]	65 ± 9	64 ± 10	ns	0.019

[a] $P = 0.007$.
[b] $P = 0.003$ basal ↓weight vs basal = /↑weight.
[c] $0.02 < P < 0.001$ CPAP vs basal, see Table 1

MetS, 2) effect of chronic (≥18 months) CPAP treatment on LV remodelling, taking into account the concomitant changes of body weight.

From our results, in patients with increased abdominal adiposity and without known cardiovascular diseases : 1) LV remodelling seems to be associated to MetS and abdominal obesity, not to OSA per se, 2) chronic CPAP treatment does not significantly influence LV remodelling, whose regression is mainly linked to body weight decrease.

Designing this study we used restrictive enrolment criteria. First, because OSA and MetS are far more frequent in subjects with increased visceral adiposity and this latter is also linked per se to LV remodelling,[24,25] we decided to enrol only overweight or obese subjects (BMI > 25 kg/m^2) with increased abdominal adiposity (waist circumference > 102 cm in men, >88 cm in women) in order to avoid the confounding effect that comes from mixing patients with and without abdominal obesity. We did not limit the enrolment to patients with BMI ≥30 kg/m^2 because increasing evidence suggests that, also in the absence of clear-cut obesity, increased abdominal fat, expressed by increased waist circumference, is associated with a higher incidence of OSA and metabolic abnormalities.[26] Patients previously or currently treated with beta-blockers and/or diuretics were excluded because these drugs can have detrimental metabolic effects, increasing per se MetS incidence.[27] We also excluded patients treated with statins that, beside lipid levels, seem able to influence BP values and possibly LV characteristics.[28] For the longitudinal study we employed another important criterion: only the patients who had not changed their drug treatment from baseline underwent the second evaluation, in order to avoid the confounding effect of new drug treatments on LV characteristics. These selection criteria greatly reduced the number of eligible patients for the cross-sectional as well as the longitudinal study, but allowed us to avoid some relevant confounding factors.

We evaluated LV remodelling by means of echocardiography, whose reliability in assessing left ventricular morpho-functional characteristics is supported by a very large body of data obtained from cross-sectional and longitudinal studies on healthy subjects and patients with many different pathologies.

High BP is a key component of MetS and influences per se LV remodelling, making a reliable assessment of BP profile very important for our purpose. Therefore, at odds with most previous studies on LV characteristics in OSA, we did not rely on clinic BP measurements, but we used 24-h ambulatory BP monitoring, more reliable in defining the actual BP burden and more correlated with target organ damage than clinic BP values.[29]

In our subjects MetS prevalence was not different among patients with mild, moderate, severe OSA and without OSA (Figure 1). This result, in agreement with some, but not all the previous studies,[16–18] indicates that the presence of MetS is not linked to OSA per se, at least in overweight/obese subjects with increased visceral adiposity.

With regard to LV remodelling, the 2 groups with MetS (OSA/MetS and noOSA/MetS) had higher LV mass index (due to greater wall thickness), lower mean values of diastolic indices and higher prevalence of LV hypertrophy and diastolic dysfunction than the 2 groups without MetS (OSA/no MetS and noOSA/noMetS). The presence of OSA was not associated to LV remodelling, whose main independent determinants were for LV mass MetS, 24-h systolic BP and age, for LV diastolic function LV mass, MetS and age, as shown by the results of multiple regression analyses. These analyses also confirmed the well known role of obesity as

Table 3 Mean values(±SD) of metabolic and LV parameters before and after CPAP treatment in patients with decreased weight (↓weight) and in patients with unchanged/increased weight (=/↑weight).

Metabolic parameters	↓ weight (n.20)		=/↑ weight (n.21)		ANOVA	
	Basal	CPAP	Basal	CPAP	CPAP	Weight change
Total Cholesterol, mg/dL	228 ± 46	217 ± 53	218 ± 39	213 ± 29	ns	ns
HDL Cholesterol, mg/dL	45 ± 10	48 ± 11	46 ± 10	48 ± 12	ns	ns
LDL Cholesterol, mg/dL	149 ± 38	142 ± 43	135 ± 34	141 ± 30	ns	ns
Triglycerides, mg/dL	165 ± 56	131 ± 57[b]	167 ± 72	163 ± 62	ns	0.016
Fasting glucose, mg/dL	100 ± 10	94 ± 8[b]	100 ± 11	102 ± 13	ns	0.010
HOMA index	3.5 ± 1.4	2.4 ± 1.5[b]	3.4 ± 1.7	3.6 ± 2.1	ns	0.014
LV parameters						
LV diastolic diameter, mm	50 ± 5	50 ± 6	49 ± 5	49 ± 4	ns	ns
Septal thickness, mm	11.6 ± 1.2	10.5 ± 0.9[b]	11.5 ± 1.4	11.6 ± 1.5	ns	0.006
Posterior wall thickness, mm	11.4 ± 1.3	10.4 ± 1.1[b]	11.1 ± 1.2	11 ± 1.3	ns	0.008
Relative wall thickness	0.46 ± 0.06	0.42 ± 0.05[b]	0.46 ± 0.08	0.46 ± 0.07	ns	0.003
LV mass index, $g/m^{2.7}$	64.7 ± 13.2[a]	55.3 ± 11.4[b]	54.9 ± 12.7	56.1 ± 12.4	ns	0.008
LV Ejection fraction, %	63 ± 4	64 ± 5	64 ± 4	65 ± 4	ns	ns
E/A	0.91 ± 0.24	1.07 ± 0.29[b]	0.95 ± 0.21	0.97 ± 0.28	ns	0.018
Em/Am	0.82 ± 0.23	0.98 ± 0.27[b]	0.93 ± 0.28	0.91 ± 0.25	ns	0.016
E′/A′	0.74 ± 0.26	0.79 ± 0.18	0.75 ± 0.26	0.76 ± 0.22	ns	ns

[a] $P < 0.05$ basal ↓weight vs basal = /↑ weight.
[b] $0.05 < P < 0.001$ CPAP vs basal see Table 2.

independent determinant of LV remodelling,[24,25] showing that BMI entered both the equations after removing MetS. Respiratory parameters did not enter the equations, meaning that they were not independent predictors of LV remodelling. We have to underline that the 4 groups were similar with regard to age, gender, BMI, waist circumference, and BP throughout the 24 h, all factors able to influence LV mass and diastolic function. Moreover the prevalence of arterial hypertension and the number of patients on chronic anti-hypertensive treatment were also similar among the 4 groups.

Besides high BP and increased visceral adiposity, other MetS components can influence the development of detrimental LV remodelling, including hyperinsulinemia and sympathetic activation, both able to stimulate myocardial cells hypertrophy and connective tissue growth.

Our results are at odds with previous studies that found greater LV mass and/or diastolic impairment in OSA patients compared to subjects without OSA.[5–7] However, in some of these studies OSA patients were older, more obese and/or with higher clinic BP than controls and, moreover, MetS presence was never evaluated.

We can not exclude that in other settings OSA could influence per se LV remodelling, but from our results MetS and abdominal obesity outweigh OSA effects on LV characteristics.

With regard to the longitudinal study, after the basal evaluation we gave advice about diet and physical activity to all the patients in order to obtain weight decrease, but, as it usually happens in clinical practice, the adherence to the advice was very different, with some patients losing weight, others maintaining the same weight or increasing it. Considering together the 41 patients who underwent the evaluation after CPAP, we could conclude, partly in agreement with some previous studies,[6,7,10,11,29] that CPAP has a positive effect on LV remodelling, inducing regression of LV hypertrophy with a modest, but statistically significant improvement of diastolic function, together with a decrease of diastolic BP and heart rate throughout the 24 h and an improvement of metabolic profile. However, when we divided the patients on the basis of weight changes, we found that only the patients who lose weight during CPAP treatment showed regression of LV hypertrophy and improvement of LV diastolic, together with decrease of 24-h diastolic BP and heart rate and improvement of metabolic profile, characterized by lower triglycerides and improved insulin sensitivity. The group of patients with unchanged/increased weight did not show any change in LV characteristics, BP values and metabolic parameters. We have to underline that at baseline all the respiratory, metabolic, BP and LV parameters were similar between the 2 groups, with the exception of BMI, waist circumference and LV mass index, higher in the group that lose weight during treatment. Moreover length of CPAP treatment, average nightly use of CPAP and extent of respiratory improvement were similar in the 2 groups. Our results are in agreement with literature data about improvement of LV characteristics after weight reduction in obese people.[19] At odds with previous studies,[6,7,10,11,30–32] in our patients CPAP treatment, beside its efficacy in improving respiratory function, seems not to exert any relevant and independent effect on LV remodelling, as well as on BP and metabolic parameters. However, our study is difficult to compare with previous ones because of some relevant differences, such as longer CPAP treatment (≥18 months), lack of changes in drug therapy during CPAP and evaluation of concomitant body weight changes.

The main limitation of our study is the relatively small number of subjects examined, due to the strict enrolment criteria employed. As a consequence some groups in the cross-sectional study and the groups evaluated in the longitudinal study were rather small, reducing

the possibility to control for significant confounders. On the other hand, the small number of patients makes more relevant the finding of statistically significant differences among the groups.

Conclusion

From our results, in overweight/obese patients LV remodelling is associated to MetS and abdominal obesity, not to OSA per se, and, probably more important, the regression of LV remodelling during CPAP treatment is driven by weight decrease, not by CPAP treatment in itself. Our findings, that need to be confirmed in larger studies, indicate that in obese patients with OSA we can not rely on CPAP treatment and consequent respiratory improvement in order to obtain regression of LV remodelling, but we have to strongly focus on dietary and lifestyle interventions in order to obtain weight decrease as the main way to improve LV characteristics.

Conflict of interest statement

None declared.

Supplementary material

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.rmed.2011.10.006.

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