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Improvement of obstructive sleep apnea does not rescue left atrial enlargement in obese participants of a multimodal weight reduction program

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Abstract

The aim of our study was to investigate the effect of obstructive sleep apnea (OSA) and its weight loss related improvement on left atrial (LA) area in individuals with severe obesity participating in a multimodal weight reduction (WR) program. Participants with obesity (body mass index, BMI, 40.2 ± 7.3 kg/m^2) underwent a 1-year WR program. Phenotyping was performed at baseline and after 12 months. Individuals were categorized according to their baseline apnea-hypopnea-index (AHI) into "no OSA" (AHI < 5) and "OSA" (AHI ≥ 5). From a total of 84 study participants, 69 completed the program. Average WR was 19.0 ± 15.7 kg after 12 months. Participants with obesity and OSA had a larger LA area at baseline as compared to participants with obesity but without OSA (22.4 ± 5.6 vs 18.8 ± 3.8 cm^2; P = .008). Linear regression showed significant associations of AHI and BMI with LA area. In contrast, despite a significant decrease of AHI in participants with OSA as compared to those without OSA at 1 year follow up (ΔAHI was −12 ± 14) ΔLA area did not significantly differ between groups. Multivariable linear regression showed no significant association of ΔAHI or ΔBMI with ΔLA. In conclusion, the presence of obstructive sleep apnea contributes to LA enlargement on top of obesity in our study cohort. Yet, successful WR with subsequently improved OSA was not associated with an improvement of LA area.

Abbreviations: A4C = apical 4-chamber view, AHI = apnea-hypopnea-index, BMI = body mass index, CCC = concordance correlation coefficient, CPAP = continuous airway pressure, LA = left atrium, LV = left ventricle, LVDD = left ventricular diastolic dysfunction, ODI = oxygen desaturation index, OSA = obstructive sleep apnea, PW = pulsed wave, WR = weight reduction.

Keywords: left atrial enlargement, obesity, obstructive sleep apnea, weight loss

1. Introduction

Changes in left atrial (LA) structure have prognostic implications. LA enlargement is associated with an increase of mortality, even in asymptomatic individuals.[1,2] Obesity and obstructive sleep apnea (OSA) are both conditions leading to LA enlargement.[3,4] In addition to frequently co-existing comorbidities like arterial hypertension, also disease-specific pathomechanisms, such as adaption to increased blood volume in obesity[3] or LA stretching due to negative intrathoracic pressure during apnea in OSA,[4] are supposed to impact on LA enlargement. This remodeling process may also be the substrate for a higher susceptibility of atrial arrhythmias like atrial fibrillation in obesity and OSA.[5,6]

OSA and obesity are both known to be associated with structural left atrial remodeling. Interestingly, it has not been investigated whether weight loss related improvement of OSA may rescue LA enlargement. Hence, the aim of our study was to investigate the effect of OSA and its weight loss related improvement on LA area in individuals with severe obesity participating in a multimodal weight reduction (WR) program.

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The datasets generated during and/or analyzed during the current study are not publicly available, but are available from the corresponding author on reasonable request.

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2. Material and methods

2.1. Study population

Individuals were participants of the "Obesity Weight Reduction and Remodeling Study,"[7–11] an ongoing prospective longitudinal study evaluating excessive body fat for its pathogenic potential in terms of cardiometabolic diseases, and the effects of a considerable WR on interactions in system´s biology. The study was approved by the Ethics Committee of the University Hospital of Regensburg.

2.2. Standardized WR program and definition of successful WR

Details of the weight loss programs have been published earlier.[10] Briefly, for the present investigation individuals with obesity aged ≥ 18 years participated either in the standardized multimodal Optifast-52 WR program (Nestlé HealthCare Nutrition GmbH, Frankfurt/Main, Germany), provided by the local Department of Psychosomatic Medicine or in a combined exercise and WR program offered by a local fitness gym.

Successful WR is defined as intentionally loosing weight of at least 10% of the initial body weight maintaining over at least 1 year.[12]

2.3. Polygraphy

An unattended home polygraphy using Stardust II (Philips Respironics, Murrysville, PA) was performed at baseline visit before starting the weight loss program as well as after 1 year of standardized WR.

Apnea was defined as a ≥ 90% decrease in airflow for ≥ 10 seconds, hypopnea as a decrease in airflow by ≥30% to 90% versus baseline for ≥10 seconds, and desaturation as a ≥4% decrease in oxygen saturation.[13,14] The apnea-hypopnea-index (AHI) was defined as the number of apneas and hypopneas per hour of sleep. The presence of ≥50% central apneas was defined as central sleep apnea and <50% central as OSA, respectively. Since none of the participants had central sleep apnea, individuals were categorized according to their baseline AHI into "no OSA" (AHI < 5) and "OSA" (AHI ≥ 5).

From the oximetry data the following parameters were extracted: oxygen desaturation index (ODI), lowest and average saturation as well as cumulative time percentage with saturation <90%. ODI is the hourly average number of desaturation episodes, which are defined as at least 4% decrease in saturation from the average saturation in the preceding 120 seconds, and lasting >10 seconds.

As we wanted to investigate the impact of *weight loss* as a sole treatment option for OSA on left atrial remodeling, participants with OSA were not concomitantly treated with *continuous airway pressure (CPAP) therapy.*

2.4. Echocardiography

Echocardiography was performed using a standard ultrasound system (Philips iE33 Philips Medical Systems, Hamburg, Germany).

2.5. LA area

LA diameter was measured in the parasternal long axis view. LA planimetry was performed in the apical 4-chamber view (A4C) at the end-ventricular systole leaving out confluences of the pulmonary veins and the LA appendage.

2.6. Echocardiographical assessment of left ventricle (LV), right atrium and right ventricle (RV)

All measurements were recorded by two expert echocardiographers. We determined the agreement between E/E´ measurements of the two expert cardiologists by the use of the concordance correlation coefficient (CCC). The CCC combines a measure for precision and accuracy to evaluate reproducibility and inter-rater reliability.[15] The CCC for 20 duplicate E/E´ measurements of the two expert sonographers was 0.976 ± 0.014 ($P < .0001$).

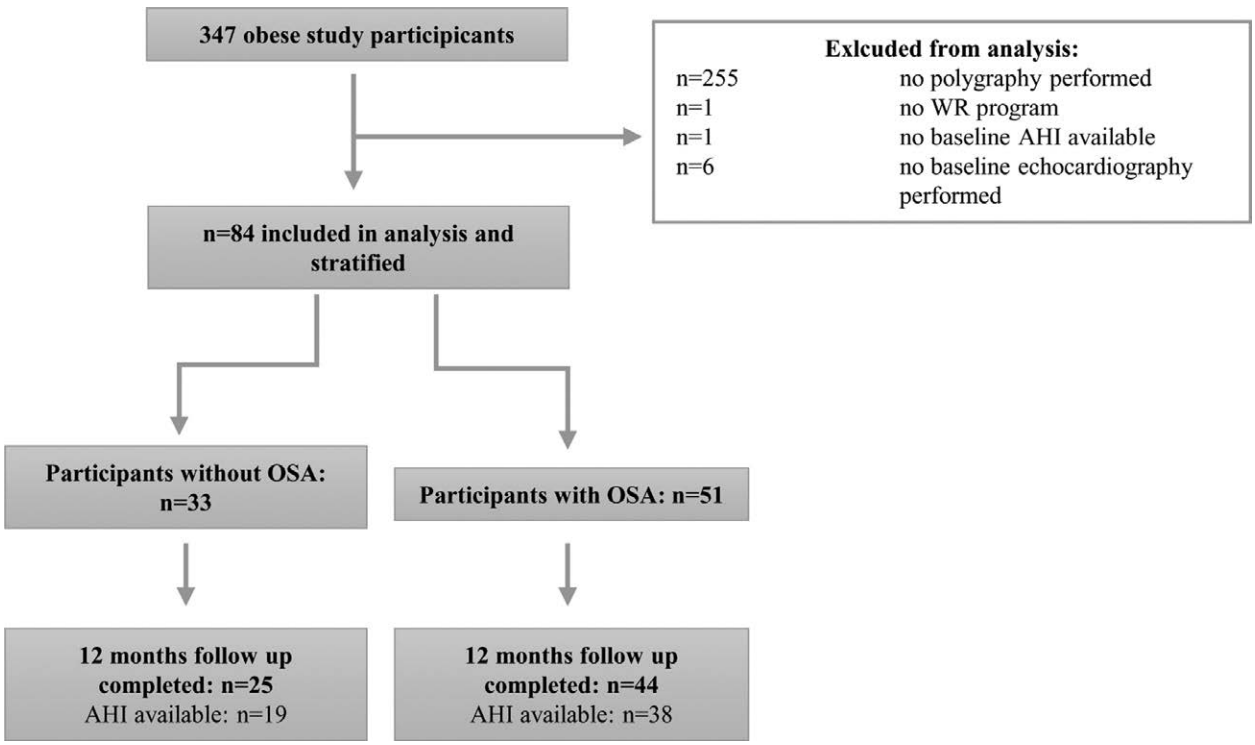

Figure 1. Study participant flow diagram. AHI = apnea-hypopnea-index, OSA = obstructive sleep apnea, WR = weight reduction.

Table 1

Clinical characteristics of study participants with and without obstructive sleep apnea at baseline.

	n	No OSA (AHI < 5)	n	OSA (AHI ≥ 5)	*P* value
Anthropometrics					
Age, y	33	40.5 ± 10.5	51	45.0 ± 11.6	.074
Sex, female, n (%)	33	25 (76)	51	26 (51)	**.023**
Caucasian, n (%)	33	33 (100)	51	51 (100)	1.000
Weight, kg	33	111.3 ± 21.9	51	125.0 ± 28.5	.052
BMI, kg/m^2	33	38.3 ± 6.5	51	41.5 ± 7.6	.07
Waist circumference, cm	33	113.3 ± 17.1	51	119.6 ± 18.5	.12
BP systolic, mm Hg	33	137 ± 13	51	143 ± 14	**.039**
BP diastolic, mm Hg	33	90 ± 9	51	93 ± 11	.19
Heart rate, bpm	33	69 ± 12	51	70 ± 11	.623
OSA parameters					
AHI (number/h)	33	2 ± 1	51	21 ± 19	**<.001**
ODI (number/h)	32	3 ± 2	48	22 ± 19	**<.001**
Mean oxygen saturation, %	33	94 ± 3	50	93 ± 3	**.037**
Minimal oxygen saturation, %	33	83 ± 6	50	78 ± 9	**.006**
Saturation < 90%, %TRT	33	8 ± 19	49	16 ± 21	**.001**
Metabolic risk markers					
Total cholesterol, mg/dL	33	201 ± 35	51	199 ± 30	.791
LDL cholesterol, mg/dL	33	120 ± 29	51	126 ± 26	.118
HDL cholesterol, mg/dL	33	51 ± 21	51	45 ± 12	.246
Triglycerides, mg/dL	33	156 ± 86	51	153 ± 84	.876
Glucose, mg/dL	33	93 ± 17	51	97 ± 25	.214
Insulin, mg/dL	33	21.0 ± 11.9	51	22.3 ± 13.6	.752
HOMA IR	33	5.0 ± 3.1	51	5.5 ± 4.1	.495
Heart failure biomarkers					
NTproBNP, pg/mL	32	46 ± 41	49	63 ± 55	.116
GDF-15, pg/mL	33	532 ± 279	50	675 ± 411	**.035**

Values represent the mean ± standard deviation or numbers (percentages). Values in bold represent significant *P* values (i.e., $P < .05$).

AHI = apnea-hypopnea-index, BMI = body mass index, BP = blood pressure, GDF-15 = growth differentiation factor 15, HDL = high density lipoprotein, HOMA-IR = homeostasis model assessment insulin resistance, LDL = low density lipoprotein, NT-proBNP = N-terminal pro brain natriuretic peptide, ODI = oxygen desaturation index, OSA = obstructive sleep apnea, WR = weight reduction.

2.7. LV geometry and function

The LV ejection fraction (EF) was measured based on the modified biplane Simpson's method. The following parameters were measured according to previous American Society of Echocardiography guidelines[16]: parasternal long axis diameter and A4C area. Measurements were done just before MV opening. LV mass (LVM) was calculated by the Devereux formula indexed to the body surface area. LV myocardial performance index (LV-MPI) was defined as the ratio of total isovolumic time (isovolumetric relaxation time (IVRT) + isovolumetric contraction time (IVCT)) divided by ejection time [(IVRT + IVCT)/ ET] using the pulsed wave (PW) Doppler method.

2.8. Parameters of LV diastolic function and definition of left ventricular diastolic dysfunction (LVDD)

Early diastolic mitral valve (MV) velocity (E) and late diastolic MV velocity (A) as well as early diastolic MV annular velocity (E´lateral) and late diastolic annular velocity (A´lateral) were measured by PW Doppler. Pulmonary vein (PV) systolic velocity (S) and PV diastolic velocity (D) were analyzed by PW Doppler. In addition, duration of reversed pulmonary vein atrial systole flow (PVa) and deceleration time (DT) of the early MV velocity were measured.

Moreover, the following ratios representing LV diastolic function were calculated: E/A, E/E´ lateral (LV filling index), E´/A´ lateral and S/D. Furthermore, we determined the difference between measured duration of reversed pulmonary vein atrial systole flow (PVa) and the duration of A (Ad).

LVDD was defined as fulfillment of the following criteria: a preserved systolic LV function (EF > 50%) and the presence of at least 2 of the following criteria consistent with abnormal LV relaxation, filling, diastolic distensibility, diastolic stiffness, or increased natriuretic peptides (N-terminal pro-brain natriuretic peptide > 220 pg/mL): E/E´ lateral > 8, E/A ≤ 0.8 together with a DT > 200 ms, PVa–Ad > 30 ms, LV mass > 149 g/m^2 (in men), >122 g/m^2 (in women) together with an enlarged LA size (LA area A4C) > 20 cm^2 or LA diameter (parasternal long axis) > 48 mm, and an E´ lateral < 10 cm/s. In contrast, subjects with a normal E´ lateral ≥ 10 cm/s together with a normal LA size were classified as having normal LV function according to the American Society of Echocardiography 2009 and European Society of Cardiology 2007 consensus criteria.[17,18]

2.9. Right heart geometry and function

Right heart geometry was evaluated by measuring RV end-diastolic (RVEDD) and end-systolic diameter (RVESD) quantified in the RV-focused view of A4C, area of the right atrium was measured in ventricular endsystole when the atrium has the largest expansion. Moreover, tricuspid annular plane systolic excursion (TAPSE), tricuspid annular systolic velocity (systolic velocity across lateral segment of tricuspid annulus; TDI S') and the tricuspid regurgitant jet velocity for estimation of systolic pulmonary artery pressure were assessed. Epicardial fat was identified as the low echo space between the outer wall of the myocardium and the visceral layer of the pericardium in the parasternal long axis view. It was measured during end-systole on the free wall of the right ventricle in a perpendicular line to the aortic annulus, used as an anatomic landmark.

2.10. Statistical analysis

Data were analyzed using the SPSS statistical software package (SPSS 23.0, IBM SPSS Statistics, Armonk, NY). Descriptive statistics are presented as the mean ± SD for continuous data

Table 2

Echocardiographic characteristics of study participants with and without obstructive sleep apnea at baseline.

	n	No OSA (AHI < 5)	n	OSA (AHI ≥ 5)	*P* value
LA parameters					
LA diameter, mm	33	41.4 ± 4.7	50	41.4 ± 8.0	.977
LA area A4C, cm^2	33	18.5 ± 3.3	50	20.8 ± 4.7	**.03**
LV parameters					
EF, %	33	66 ± 6	50	66 ± 6	.852
LV-MPI	33	0.68 ± 0.14	50	0.73 ± 0.42	.5
IVS, mm	33	10.3 ± 1.8	50	11.2 ± 1.5	**.011**
PW, mm	33	10.2 ± 1.3	50	10.5 ± 1.2	.421
LVEDD, mm	33	51 ± 5	50	52 ± 5	.591
LVESD, mm	33	30 ± 4	50	32 ± 5	.08
LVM, g/m^2	33	113.6 ± 24.3	49	118.1 ± 24.1	.467
Right heart parameters					
RA area, cm^2	32	20.0 ± 7.3	50	19.9 ± 5.5	.956
RVEDD, mm	33	32 ± 5	49	32 ± 5	.61
RVESD, mm	33	22 ± 4	49	22 ± 4	.408
S´, cm/s (TV annular velocity)	30	12.5 ± 2.4	50	13.4 ± 2.0	.064
TAPSE, mm	31	26 ± 3	50	26 ± 6	.572
PAP, mm Hg	13	21 ± 5	11	19 ± 7	.475
Epicardial fat, mm	33	5.6 ± 1.8	50	6.4 ± 1.7	.055
Diastolic function parameters					
Diastolic dysfunction, n (%)	32	0 (0)	48	5 (9.8)	.059
E/A ratio	33	1.3 ± 0.4	50	1.1 ± 0.3	.077
E/E´ ratio	33	6.9 ± 1.5	50	7.1 ± 2.2	.585
E´/A´ ratio	33	1.5 ± 0.7	50	1.3 ± 0.6	.075
Deceleration time, ms	33	190 ± 51	49	180 ± 43	.38
S/D ratio	32	1.2 ± 0.2	50	1.2 ± 0.3	.397
PVa duration – A duration, ms	31	−42 ± 33	48	−47 ± 34	.515
Mitral regurgitation, n (%)	31	14 (45)	48	19 (40)	.624

Values represent the mean ± standard deviation or numbers (percentages). Values in bold represent significant *P* values (i.e., $P < .05$).

A = late diastolic MV velocity, A4C = apical 4 chamber view, AHI = apnea-hypopnea-index, EF = ejection fraction, E/A = ratio of early diastolic MV velocity/late diastolic MV velocity, E´/A` = ratio of early diastolic MV annular velocity/late diastolic MV annular velocity, E/E´ = ratio of early diastolic MV velocity/early diastolic MV annular velocity, IVS = interventricular septum, LA = left atrial, LVEDD = left ventricular end-diastolic diameter, LVESD = left ventricular end-systolic diameter, LVM = left ventricular mass, LV-MPI = left ventricular myocardial performance index, OSA = obstructive sleep apnea, PAP = pulmonary artery pressure, PVa = pulmonary venous atrial reversal, PW = posterior wall, RA = right atrial, RVEDD = right ventricular end-diastolic diameter, RVESD = right ventricular end-systolic diameter, S´ = systolic tricuspid valve annular velocity, S/D = ratio of systolic pulmonary venous velocity/diastolic pulmonary venous velocity, TAPSE = tricuspid annular systolic plane excursion.

Table 3

Uni- and multivariable regression analysis left atrial area.

		Unadjusted		Adjusted for BMI or AHI, respectively, sex, systolic blood pressure	
Independent	**Dependent**	**ß coefficient**	***P* value**	**ß coefficient**	***P* value**
Model 1: Cross-sectional analysis of AHI and BMI, respectively, and LA area					
AHI	LA area A4C	0.454	**<.001**	0.246	**.014**
BMI	LA area A4C	0.420	**<.001**	0.355	**<.001**
		Unadjusted		**Adjusted for ΔBMI or ΔAHI, respectively, age and Δsystolic blood pressure**	
Independent	**Dependent**	**ß coefficient**	***P* value**	**ß coefficient**	***P* value**
Model 2: Longitudinal analysis of ΔAHI and ΔBMI, respectively, and ΔLA area					
ΔAHI	ΔLA area A4C	0.112	.431	0.128	.410
ΔBMI	ΔLA area A4C	0.05	.727	0.158	.397

Values in bold represent significant *P* values (i.e., $P < .05$).

A4C = apical 4 chamber view, AHI = apnea-hypopnea-index, BMI = body mass index, LA = left atrium.

and as number and percentages for categorical data. Shapiro–Wilk was used to test for normal distribution. Student *t* test was used to assess linear trends of parameters for normal and independent data. Skewed data were evaluated by the Mann–Whitney *U* test. Linear regression models were calculated to assess the predictive value of AHI/ΔAHI and body mass index (BMI)/ΔBMI with respect to LA area/ΔLA area. Multiple linear regression model was adjusted for possible confounders that included age, sex and systolic blood pressure. Confounding variables were those that conferred at least a 10% change in the β-coefficient for delta BMI when added to the model.[19] Scatter plots with regression lines were used to visualize the relationship between variables. All reported *P* values are two-sided, with .05 considered the threshold for statistical significance.

3. Results

From a total of 84 study participants with obesity there were 33 without (AHI < 5 events per hour) and 51 with OSA (AHI ≥ 5 events per hour). 69 study participants (82%) completed the program (Fig. 1). Age at baseline ranged from 18 to 73 years, and BMI from 30.1 to 58.6 kg/m^2.

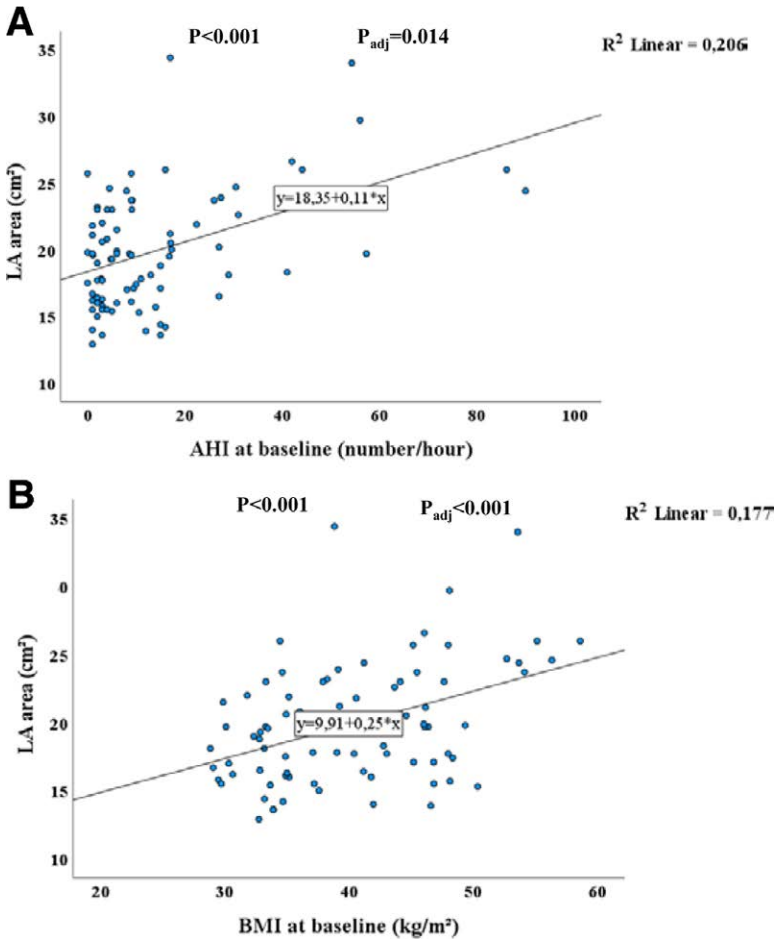

Figure 2. Scatter plots demonstrating significant relationship between AHI at baseline and LA area (A) as well as BMI at baseline and LA area (B). AHI = apnea-hypopnea-index, BMI = body-mass-index, LA = left atrial.

3.1. Clinical characteristics at baseline

Baseline clinical characteristics are displayed in Table 1. Individuals with OSA were more often male with higher systolic blood pressure levels compared to those without OSA. ODI, minimal oxygen saturation and proportion of saturation < 90% were unfavorably altered in obese participants with OSA. There were no significant differences between the groups concerning parameters of lipid and glucose metabolism at baseline. Only growth differentiation factor 15 (GDF-15) levels were significantly higher in obese participants with OSA.

3.2. Echocardiographic characteristics at baseline

Echocardiographic characteristics at baseline are described in Table 2. LA area was significantly increased in individuals with OSA (LA area 20.8 ± 4.7 vs 18.5 ± 3.3 cm^2; P = .03). Interventricular septum was thicker in the OSA group, beyond that no significant differences with respect to left ventricular (LV) systolic and diastolic function as well as right heart parameters were observed. The percentage of patients with mitral regurgitation (all grade 1) was not significantly different between groups. A non-significant trend towards greater epicardial fat thickness and higher percentage of diastolic dysfunction could be observed in individuals with OSA.

Linear regression analysis showed a significant association between both AHI and BMI with LA area, respectively (LA area: R^2=0.206 vs R^2= 0.177; Table 3 model 1 and Fig. 2). After adjusting for significant confounders these associations remained significant (LA area: ß 0.246, P = .014 for AHI; ß 0.355, P < .001 for BMI; Table 3).

3.3. Clinical characteristics at follow up

At 1-year follow up participants in both groups had reduced their weight significantly as compared to baseline (112.1 ± 20.2 vs 97.3 ± 18.6 kg, P < .001 in individuals without OSA; 126.1 ± 29.9 vs 104.7 ± 22.2 kg; P < .001 in individuals with OSA). Successful WR was achieved in 52% of individuals without OSA and in 68% of individuals with OSA without significant difference between groups (P = .182). After 1 year of follow-up, 9 out of 25 participants (36%) in the group without OSA were no longer obese, compared with 8 out of 44 participants (18%) in the group with OSA. The changes of clinical characteristics from baseline to follow up are shown in Table 4. At 1-year follow up, ΔAHI was −12 ± 14 in individuals with OSA, while ΔAHI was 0 ± 2 in individuals without OSA (P < .001). Anthropometric data as well as metabolic and heart failure biomarkers were similar in both groups.

3.4. Echocardiographic characteristics at follow up

The changes of echocardiographic measures from baseline to follow up are displayed in Table 5. With respect to LA structure, ΔLA area did not differ between groups (0.1 ± 3.5 cm^2 in individuals without OSA vs −1.0 ± 4.1 cm^2 in individuals with OSA, P = .151). Changes of LV, right heart and diastolic function parameters were similar in both groups.

Longitudinal analysis of ΔAHI and ΔBMI with ΔLA area revealed no significant association (Table 3, model 2).

4. Discussion

Our current study shows that improvement in AHI following moderate weight loss is not associated with a reduction of

Table 4

Deltas (follow up vs baseline) of clinical characteristics of study participants with and without obstructive sleep apnea.

	FU n = 25		FU n = 44		
	n	No OSA (AHI < 5)	n	OSA (AHI ≥ 5)	*P* value
Anthropometrics					
Weight, kg	25	−14.8 ± 13.0	44	−21.4 ± 16.7	.09
BMI, kg/m^2	25	−5.1 ± 4.1	44	−7.0 ± 5.5	.13
Waist circumference, cm	25	−10.8 ± 11.9	44	−12.8 ± 14.5	.568
BP systolic, mm Hg	24	−8 ± 13	44	−7 ± 14	.408
BP diastolic, mm Hg	24	−7 ± 9	44	−6 ± 10	.386
Heart rate, bpm	25	−8 ± 16	44	−6 ± 12	.553
Successful WR, n (%)	25	13 (52)	44	30 (68)	.182
OSA parameters					
AHI (number/h)	19	0 ± 2	38	−12 ± 14	**<.001**
Metabolic risk markers					
Total cholesterol, mg/dL	25	−4 ± 41	44	−9 ± 34	.655
LDL cholesterol, mg/dL	25	−9 ± 30	44	−7 ± 27	.951
HDL cholesterol, mg/dL	25	5 ± 12	44	6 ± 10	.906
Triglycerides, mg/dL	25	−11 ± 118	44	−27 ± 81	.510
Glucose, mg/dL	25	−5 ± 15	44	−10 ± 27	.461
Insulin, mg/dL	25	−6.1 ± 14.4	44	−7.8 ± 10.6	.618
HOMA IR	25	−1.7 ± 3.7	44	−2.3 ± 3.9	.513
Heart failure biomarkers					
NTproBNP, pg/mL	23	18 ± 32	43	31 ± 112	.505
GDF-15, pg/mL	8	−126 ± 136	21	−79 ± 198	.545

Values represent the mean ± standard deviation. Values in bold represent significant *P* values (i.e., $P < .05$).

AHI = apnea-hypopnea-index, BMI = body mass index, BP = blood pressure, FU = follow up, GDF-15 = growth differentiation factor 15, HDL = high density lipoprotein, HOMA-IR = homeostasis model assessment insulin resistance, LDL = low density lipoprotein, NT-proBNP = N-terminal pro brain natriuretic peptide, OSA = obstructive sleep apnea, WR = weight reduction.

Table 5

Deltas of echocardiographic parameters of study participants with and without OSA.

	n	No OSA (AHI < 5)	n	OSA (AHI ≥ 5)	*P* value
LA parameters					
LA diameter, mm	25	−0.9 ± 7.3	41	0.6 ± 9.0	.17
LA area A4C, cm^2	25	0.1 ± 3.5	41	−1.0 ± 4.1	.151
LV parameters					
EF, %	25	−1 ± 8	41	−2 ± 8	.457
LV-MPI	25	−0.08 ± 0.18	38	−0.01 ± 0.21	.216
IVS, mm	25	−0.3 ± 1.4	41	−0.5 ± 1.4	.293
PW, mm	25	−0.3 ± 1.4	41	0.0 ± 1.4	.37
LVEDD, mm	25	−1 ± 5	41	1 ± 5	.322
LVESD, mm	25	1 ± 5	41	2 ± 4	.111
LVM, g/m^2	23	−2.5 ± 23.6	40	8.5 ± 25.0	.089
Right heart parameters					
RA area, cm^2	24	−1.9 ± 5.4	42	−1.8 ± 5.5	.979
RVEDD, mm	24	−4 ± 12	41	−5 ± 13	.74
RVESD, mm	24	0 ± 9	41	−2 ± 10	.495
S´, cm/s (TV annular velocity)	21	−1.4 ± 2.4	41	−1.8 ± 2.4	.576
TAPSE, mm	21	−2 ± 5	41	−2 ± 6	.941
PAP, mm Hg	6	−5 ± 5	8	1 ± 6	.08
Epicardial fat, mm	25	5.6 ± 1.8	41	6.4 ± 1.7	.931
Diastolic function parameters					
E/A ratio	25	0.0 ± 0.3	41	0.1 ± 0.4	.372
E/E´ ratio	25	0.0 ± 2.4	41	0.9 ± 3.5	.276
E´/A´ ratio	25	0.1 ± 1.0	41	0.0 ± 0.5	.369
Deceleration time, ms	25	−11 ± 52	41	7 ± 59	.201
S/D ratio	24	0.0 ± 0.3	41	0.0 ± 0.3	.547
PVa duration – A duration, ms	25	−6 ± 45	40	−16 ± 63	.501

Values represent the mean ± standard deviation.

A = late diastolic MV velocity, AHI = apnea-hypopnea-index, E/A = ratio of early diastolic MV velocity/late diastolic MV velocity, E/E´ = ratio of early diastolic MV velocity/early diastolic MV annular velocity, E´/A´ = ratio of early diastolic MV annular velocity/late diastolic MV annular velocity, EF = ejection fraction, IVS = interventricular septum, LA = left atrium, LVEDD = left ventricular end-diastolic diameter, LVESD = left ventricular end-systolic diameter, LVM = left ventricular mass, LV-MPI = left ventricular myocardial performance index, MV = mitral valve, OSA = obstructive sleep apnea, PAP = pulmonary artery pressure, PVa = pulmonary venous atrial reversal, PW = posterior wall, RA = right atrial, RVEDD = right ventricular end-diastolic diameter, RVESD = right ventricular end-systolic diameter, S/D = ratio of systolic pulmonary venous velocity/diastolic pulmonary venous velocity, S´ = systolic tricuspid valve annular velocity, TAPSE = tricuspid annular systolic plane excursion.

LA area in obese study participants after 12 months follow up.

LA enlargement in individuals with OSA has been described before,[20–25] especially in the presence of obesity.[26–28] Whereas

obesity related LA dilation may be a consequence of adaptive processes owing to LVDD as well as increase of blood volume,[3] OSA mediated LA dilation is assumed to involve LVDD independent mechanisms, namely LA stretching due to excess of negative intrathoracic pressure during apnea.[4] Supporting this hypothesis, Imai et al found that the extent of LA enlargement depends on the severity of OSA as an independent parameter of left atrial volume index (LAVI) after adjusting for important confounders including LVDD parameters.[23] Likewise, Otto et al reported higher LAVI in individuals with obesity and OSA compared to those without OSA.[26] In our study population, neither LVDD parameters nor proportion of individuals with LVDD differed between groups. However, linear regression analysis still confirmed a significant relationship between AHI and LA area in our study population as well, even after adjusting for LVDD (data not shown).

In contrast, interventional studies investigating the effect of OSA treatment on LA area are rare. To the best of our knowledge, our study is the first to evaluate the impact of weight loss related OSA improvement on LA area. Linear regression analysis failed to show a significant relationship between an improvement in AHI and a reduction of LA area. Furthermore, ΔLA area was not different in individuals with and without OSA at 12 months follow up. In line with this, a retrospective analysis of CPAP-compliant versus CPAP non-compliant OSA patients reported only a non-significant trend to a reduction of LAV and LAVI in compliant patients after ~10 months post CPAP intervention, whereas non-compliant patients experienced a further LA enlargement.[29] Taken together, these observations suggest that OSA treatment may not necessarily improve LA structure, but may at least prevent the progression of further structural remodeling within a rather short time frame of ~1 year.

Several limiting factors of our study results should be mentioned. First, the relatively small sample size of our study could result in a lack of power showing differences between groups. As LA planimetry was the standard parameter of assessing LA geometry at the time of study conduction, LAV and LAVI were not determined. As LAVI is a more valuable prognostic parameter regarding cardiovascular outcome compared to LA area,[30] this might restrict the interpretation of our data. Moreover, a further classification of individuals according to OSA severity was not possible due to the small cohort size. Although all data were gathered prospectively, categorizing in individuals with and without OSA was performed retrospectively. Furthermore, interpretation of our results could be complicated by the presence of two possible weight loss interventions (70% Optifast-52, 30% WR fitness gym). However, adjusting P values for type of weight reduction did not change results. Furthermore, 82% of participants with OSA remained obese at 12 months, so we cannot exclude the possibility that there is a threshold from which a further reduction in weight towards normal weight might have positive effects on LA remodeling. Finally, limited testing conditions in individuals with extreme obesity could impact our results.

In conclusion, our study shows that obstructive sleep apnea may contribute to LA enlargement on top of obesity. However, treatment of OSA through moderate WR was not associated with an improvement of LA area in our study.

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