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Left ventricular diastolic dysfunction is linked to severity of obstructive sleep apnea

Running head: diastole and sleep apnea

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Abstract (Word count: 199)

Background Obstructive sleep apnea has been related to increased cardiovascular risk. The present study examined the relationships between respiratory parameters and left ventricular abnormalities in obstructive sleep apnea.

Patients/Methods One hundred and fifty newly diagnosed OSA patients without any known cardiovascular disease were included (age = 49±11 years, BMI = 27.1±3.3 kg/m², respiratory disturbance index = 41±18/h). Haemodynamic, biological, respiratory, cardiac and arterial parameters were assessed at inclusion.

Results Thirty-four patients (22.7%) had a grade 1 left ventricular diastolic dysfunction. Patients with an abnormal diastole were older ($p<0.001$) and 81% of them were hypertensive. The only respiratory parameter independently associated with the E/A ratio was mean nocturnal oxygen saturation. Seventeen patients (13%) had left ventricular hypertrophy. A multivariate analysis showed that clinic systolic blood pressure and mean nocturnal oxygen saturation were independently associated with left ventricular hypertrophy. In a logistic regression model, an age $\geq$ 58 years (OR 3.29, 95% CI 1.78-5.64) and mean nocturnal oxygen saturation < 92% (OR 2.76, 95% CI 1.45-4.91) were associated with left ventricular diastolic dysfunction.

Conclusion Our findings demonstrate that left ventricular diastolic dysfunction frequently occurs in patients with obstructive sleep apnea and that it is related to the severity of oxygen desaturation.

Keywords: Diastole, Echocardiography, Hypertension, Left ventricular hypertrophy, Sleep apnea

Abbreviations list

A	Peak flow velocity at atrial contraction
ABPM	Ambulatory blood pressure monitoring
BMI	Body mass index
BP	Blood pressure
BSA	Body surface area
CAD	Coronary artery disease
CI	Confidence interval
CPAP	Nasal continuous positive airway pressure
DBP	Diastolic blood pressure
DT	Mitral deceleration time
E	Peak flow velocity in early diastole
HR	Heart rate
IVS	Interventricular septum thickness
LV	Left ventricular
LVD	Left ventricular internal end-diastolic diameter
LVEF	Left ventricular ejection fraction
LVH	Left ventricular hypertrophy
LVM	Left ventricular mass
LVMI	Left ventricular mass index
LVPW	Left ventricular posterior wall thickness
LVS	Left ventricular internal end-systolic diameter
OR	Odds ratio
OSA	Obstructive sleep apnea

PP	Pulse pressure
PWV	Carotid-to-femoral pulse wave velocity
RDI	Respiratory disturbance index
SaO2	Oxygen saturation
SBP	Systolic blood pressure

Introduction

Obstructive sleep apnea (OSA) is a common but underestimated disease that has been related to increased cardiovascular risk [1]. Thus, hypertension, coronary artery disease (CAD), rhythm/conduction problems and cerebrovascular diseases are often present in apneic patients, all the more so if the OSA is severe [2-5]. Morbidity and mortality connected to OSA are reduced by treatment with nasal continuous positive airway pressure (CPAP) [6]. The main mechanisms connected to OSA and involved in the genesis of cardiovascular diseases are sympathetic hyperactivity, endothelial dysfunction, systemic inflammation, insulin resistance, oxidative stress and coagulation anomalies [7-9].

Sleep apnea is often found in patients with heart failure [10]. However, the combination of sleep apnea and heart failure is different to the previously mentioned combinations (i.e. OSA with hypertension or CAD) as the majority of the sleep apnea cases are central or mixed in heart failure patients. OSA can nonetheless lead to heart failure – systolic heart failure as after a myocardial infarction, or diastolic heart failure as is often the case in hypertensive patients. Almost half of heart failure patients have a preserved systolic function, i.e. a left ventricular (LV) ejection fraction (LVEF) $\geq$ 45%. Diastolic anomalies appear to be common in OSA, but the majority of studies in this area have been carried out on small patient populations [11-14]. Left ventricular hypertrophy (LVH) often seems to be associated with this LV diastolic dysfunction [15].

The purpose of this study was to determine the relationship between respiratory variables on the one hand and LV diastolic parameters and LVH on the other hand in a large population of newly diagnosed OSA patients without any known cardiovascular disease.

Materials and Methods

Study subjects

One hundred and fifty patients referred to the Grenoble University Hospital sleep laboratory for symptoms indicating OSA were included between November 2001 and July 2007. They were either recruited from the sleep laboratory where they underwent full polysomnography or from the ward sleep unit where the diagnosis of OSA was confirmed by simplified polygraphy without electroencephalogram (EEG) recordings. None of the patients had any known cardiovascular disease and none of them were receiving any vasoactive treatment. We used the following exclusion criteria: diseases potentially affecting blood pressure (BP) regulation (e.g. Parkinson's disease, renal or cardiac transplantation, heart failure and diabetes mellitus); atrial fibrillation or frequent premature beats ($\geq$ 10/min), patients suffering from respiratory insufficiency and previous treatment of OSA. Ethical approval was obtained from the local ethics committee and all of the participants gave their informed consent. The registration (ClinicalTrials.gov) trial number for this study is: NCT00764218.

Blood pressure and heart rate measurements

Clinic BP was measured according to ESH-ESC guidelines [16]. The following parameters were assessed: systolic BP (SBP), diastolic BP (DBP) and pulse pressure (PP). Clinic hypertension was defined as a clinic SBP $\geq$ 140 mmHg and/or a clinic DBP $\geq$ 90 mmHg. Clinic heart rate (HR) was measured by pulse palpation (30 s) in the lying position. Ambulatory BP monitoring (ABPM) was carried out with a Spacelabs 90207® device (Spacelabs International, Redmond, Washington, USA). The measurements were made every 15 minutes over 24 hours. Daytime (7.00 am to 10.00 pm) hypertension was

defined as daytime SBP ≥ 135 mmHg and/or daytime DBP ≥ 85 mmHg, and nocturnal (10.00 pm to 7.00 am) hypertension as nocturnal SBP ≥ 120 mmHg and/or nocturnal DBP ≥ 70 mmHg [16]. Dipper pattern was defined by a nocturnal fall of BP ≥ 10%.

Respiratory measurements

Full polysomnography was performed in 108 of the 150 patients (72%). Continuous recordings were taken with electrode positions C3/A2-C4/A1-Cz/01 of the international 10-20 Electrode Placement System, eye movements, chin electromyogram and ECG modified V2 lead. Sleep was scored manually according to standard criteria [17]. Airflow was measured using nasal pressure associated with the sum of buccal and nasal thermistor signals. Respiratory efforts were monitored with abdominal and thoracic bands. An additional signal of respiratory effort (i.e. pulse transit time) was recorded concurrently. Pulse transit time allowed us to identify "autonomic activations" and as a consequence micro arousals [18]. Thus, we were able to use the same rules and definition for hypopneas whatever the diagnosis technique we used for diagnosing sleep apnea. Oxygen saturation (SaO2) was measured using a pulse oximeter (Biox-Ohmeda 3700®, Ohmeda, Liberty Corner, NJ, USA). The same variables were measured in the remaining 42 patients except for sleep variables which were not recorded. An apnea was defined as a complete cessation of airflow for ≥ 10 seconds, and a hypopnea as a ≥ 50% reduction in the nasal pressure signal or a 30% to 50% decrease associated with either oxygen desaturation of ≥ 3% or an arousal (defined according to the Chicago report or by autonomic activations on pulse transit time), both lasting for ≥ 10 seconds [18-19]. Apneas were classified as obstructive, central or mixed according to the presence or absence of respiratory efforts. The classification of hypopneas as obstructive or central

was based upon the pulse transit time signal and the shape of the inspiratory part of nasal pressure. A respiratory disturbance index (RDI) was calculated and defined as the number of apneas and hypopneas per hour of sleep (full polysomnography) or per hour of recording (polygraphy without EEG recording). In our study, diagnosis of OSAS was retained if RDI $\geq$ 15 per hour.

Echocardiography

The echocardiogram was carried out using a HP Sonos 2500® (Hewlett Packard, Santa Clara, Ca, USA) machine equipped with a 2.5 MHz probe. The examination was performed in M-mode with 2D guidance in the long axis of the left parasternal view. LV internal end-diastolic (LVD) and end-systolic diameters, as well as interventricular septum (IVS) and posterior wall (LVPW) thicknesses, were measured over five consecutive cycles. Systolic function was assessed by the LVEF according to the Teicholz formula. LV mass (LVM) was measured according to the Penn convention using the Devereux formula and was normalized for body surface area (BSA) and for height$^{2.7}$ to derive the LV mass index (LVMI) [20]. LVH was defined as a LVMI of $\geq$ 111 g/m² or $\geq$ 50 g/m$^{2.7}$ in men and of $\geq$ 106 g/m² or $\geq$ 47 g/m$^{2.7}$ in women [21]. Left atrial end-systolic diameter was measured in M-mode in the parasternal long axis view. LV diastolic function was evaluated by transmitral Doppler using pulsed Doppler technique with 2D guidance in apical four-chamber view [16, 22]. The following diastolic parameters were measured or calculated from at least three consecutive beats: E wave (peak flow velocity in early diastole); A wave (peak flow velocity at atrial contraction); and the E/A ratio. The mitral deceleration time (DT) and the Valsalva manoeuvre were used to distinguish the different filling patterns if necessary. A normal

pattern was defined by an E/A ratio > 1 and normal DT (160 to 240 ms); impaired relaxation was defined by an E/A ratio < 1 and DT > 240 ms; a pseudonormal pattern by an E/A ratio ranging from 1 to 1.5, DT > 240 ms and reversal of the E/A ratio (to < 1.0) by Valsalva manoeuvre; and a restrictive pattern by an E/A ratio > 1.5 and DT < 160 ms. All echocardiograms were performed by the same experienced echocardiographer.

Aortic pulse wave velocity

To determine the carotid-to-femoral pulse wave velocity (PWV), two pulse transducers were fixed on the skin over the right common carotid and femoral arteries. The time delay was measured with a Complior® device (Artech Medical, Pantin, France), between the feet of simultaneously recorded pulse waves and averaged over 10 consecutive cycles. The carotid-femoral PWV was calculated as the distance between the arterial sites divided by the time delay.

Biological parameters

All the subjects had plasma measurements (enzymatic colorimetry) taken of total cholesterol normal, triglycerides, HDL cholesterol, LDL cholesterol (Friedwald formula), glucose and creatinine.

Statistical analysis

Statistical analyses were performed using SPSS software (SPSS Inc, Chicago, IL, USA). Normality of data distribution was assessed. Continuous data were expressed as mean+/-SD. Relationships between the continuous variables were evaluated by Pearson's correlation analysis when data were normally distributed or by Spearman's

correlation analysis when they were not normally distributed. Non-continuous variables were compared using a Chi² test. Comparisons between groups for continuous variables were made using a Student's T test (or Mann-Whitney test when the data were not normally distributed). Multivariate analysis was performed by a stepwise regression. Variables included in our analysis were all the variables significantly ($p<0.05$) associated with the explained variable using univariate analysis. Odds ratios (OR) were calculated using a logistic regression method to assess the significant association between a LV diastolic dysfunction on the one hand and parameters of OSA severity or other cardiovascular risk factors on the other hand. All OR are presented with their 95% confidence intervals (95% CI). Values of $p<0.05$ were considered significant for all analyses.

Results

General data

The anthropometric, biological and haemodynamic characteristics of the global cohort are presented in Table 1. ABPM was valid for both daytime and nocturnal periods in 135 of the 150 patients (90%). Twenty-seven subjects (18%) were obese, 102 (76%) were hypertensive (in clinic or in ABPM), 54 (36%) had clinic hypertension, 71 (53%) had daytime hypertension and 93 (69%) had nocturnal hypertension. The respiratory, cardiac and arterial characteristics of the global population are presented in Table 2.

LV diastolic function

Thirty-four of the 150 patients (22.7%) had an impaired LV relaxation. Patient characteristics according to whether or not they had a diastolic dysfunction are presented in Tables 1 and 2. Patients with a diastolic dysfunction were older and had higher clinic BP and HR readings. Eighteen of them (53%) had clinic hypertension and 26 (81%) had abnormal ABPM. There was a trend to find more LV diastolic dysfunction in subjects with hypertension than in normotensives (33% vs 23% respectively, p=0.11).

Prevalence of nocturnal hypertension was higher in patients with impaired LV diastolic function than in those with normal LV function (80% vs. 67%, p=0.042). Half of the patients with impaired LV relaxation had a non-dipper pattern (vs. 42% if normal LV function, p=0.71).

If there was diastolic dysfunction, LVMI-height$^{2.7}$ and PWV were higher and mean nocturnal SaO2 was lower (Figure 1). In the global population, a correlation analysis showed that the E/A ratio was significantly related to age (r=-0.52, p< 0.001), clinic DBP (r=-0.27, p=0.001) and SBP (r=-0.26, p=0.002), PWV (r=-0.24, p=0.007), RDI (r=-0.18, p=0.027) and mean nocturnal SaO2 (r=0.41, p<0.001, Figure 2) but not to LVMI-height$^{2.7}$. In the subgroup of normotensive subjects, E/A ratio was significantly correlated to age (r=-0.56, p<0.001), mean nocturnal SaO2 (r=0.47, p<0.001) and clinic DBP (r=-0.21, p=0.038).

A stepwise regression analysis showed that in the whole population the only respiratory parameter independently associated with the E/A ratio was mean nocturnal SaO2 (beta=0.29, p=0.001). A logistic regression model showed that an age $\geq$ 58 years (OR

3.29, 95% CI 1.78-5.64) and a mean nocturnal SaO2 < 92% (OR 2.76, 95% CI 1.45-4.91) were associated with a LV diastolic dysfunction.

LV mass

Cardiac ultrasound was valid for LV dimensions in 132 of the 150 patients (88%). All the patients had a LVEF $\geq$ 45% and 27 subjects (18%) had a left atrial dilation (diameter $\geq$ 40 mm). Patients with a LVH-height$^{2.7}$ (N=17, 13%) had a higher 24-hour SBP (134$\pm$13 vs 122$\pm$13, p=0.003), a lower mean nocturnal SaO2 (91.9$\pm$3.1 vs 93.7$\pm$1.6, p<0.001) and a higher RDI (47.0$\pm$17.1 vs 37.9$\pm$15.3, p=0.033). LVMI-BSA and LVMI-height$^{2.7}$ were correlated to the BP parameters (r=0.41, p<0.001 for LVMI-height$^{2.7}$ and nocturnal PP). Among patients with LVH, 91% had nocturnal hypertension (vs. 67% in subjects without LVH, p=0.088) and 46% were non dippers (vs. 43% if absence of LVH, p=0.55). The LVMI-height$^{2.7}$ was similar in dipper and non-dipper groups (38.0$\pm$8.5 vs. 39.3$\pm$7.7 g/m, respectively, p=0.39). There was a significant correlation between LVMI-height$^{2.7}$ on the one hand and mean nocturnal SaO2 (r=-0.30, p=0.001, Figure 2), minimal nocturnal SaO2 (r=-0.23, p=0.01), RDI (r=0.21, p=0.015) and age (r= 0.18, p=0.034) on the other hand. A multivariate analysis revealed that clinic SBP (beta=0.30, p=0.001) and mean nocturnal SaO2 (beta=-0.26, p=0.003) were independently associated with LVMI-height$^{2.7}$.

Discussion

Unlike most of the studies previously published in the field, our results came from a large cohort of newly diagnosed OSA patients, essentially non obese, unknown to be hypertensive before the inclusion in the study, none of them receiving any vasoactive

medications and in whom 24-hour ABPM has been systematically performed. Our study is unique not only because main confounders were discarded but also because a complete cardiovascular phenotype was obtained in the all set of patients.

The main results of our study are as follows: 1) nearly one quarter of OSA patients had a LV diastolic dysfunction; 2) more severe was OSA, higher was the prevalence of LV diastolic dysfunction; 3) the only respiratory parameter independently associated with the E/A ratio was mean nocturnal SaO2; 4) clinic SBP and mean nocturnal SaO2 were the only variables independently associated with LVMI-height$^{2.7}$.

Left ventricular diastolic dysfunction

As we previously published in a subset of the same cohort, the prevalence of hypertension evidenced by ABPM is very high in OSA subjects even supposed to be free of cardiovascular consequences [23]. Morbidity and mortality in heart failure patients with preserved LV systolic function (i.e. diastolic dysfunction) is high. Hypertension, diabetes mellitus, LVH, myocardial ischemia and LV systolic dysfunction are frequently associated with diastolic dysfunction. OSA is frequent in heart failure patients [24]. Conversely, the presence of OSA led to an increase in the likelihood of having heart failure, independently of other known risk factors [25].

The methods used to analyse LV diastole vary from one published study to another. We have chosen a simple and validated index, the E/A ratio, combined with a measurement of the DT of the E wave and with the performance of a Valsalva manoeuvre. We found a high prevalence (23%) of LV diastolic dysfunction (impaired relaxation pattern). This therefore shows that in newly diagnosed OSA patients, there is essentially a LV relaxation anomaly. In our study, patients with a LV diastolic dysfunction were older

with a higher clinic BP, LVMI and aortic stiffness. As in our study, Arias et al, found a high prevalence (56%) of abnormal LV filling patterns in 27 OSA patients, with a majority of subjects suffering from an impaired relaxation pattern [12]. On the contrary, in 353 apneic patients, Niroumand et al. concluded that OSA is not independently associated with impaired LV diastolic function evaluated by the E/A ratio [26]. However, in this last study, patients were obese and 21% were known to be hypertensive upon inclusion. In the Arias' study, the RDI was the only predictive factor of LV diastolic dysfunction [12]. Importantly, more severe OSA is associated with a higher degree of LV diastolic dysfunction [11, 27]. Using Doppler tissue imaging, several authors found an independent relationship between OSA severity and LV diastolic parameters (mitral annulus velocities) [14]. Our study, which was performed on a larger cohort of OSA patients than most of the studies cited above, demonstrates that only mean nocturnal SaO2 is independently linked to E/A ratio. Moreover, we found that a mean nocturnal SaO2 < 92% led to a 2.76 increase in the likelihood of suffering from a LV diastolic dysfunction. As a single value, minimal nocturnal SaO2 is not at all reflecting the overall nocturnal hypoxemia and then is frequently, as in our study for the LV diastolic function, unrelated to cardiovascular or metabolic consequences. Time spent at a SaO2 below 90% is an interesting indicator of the amount of desaturations. However, as our patients were lean and exhibited moderate to severe OSA, a significant proportion of them (24%) had 0% of time spend below 90% of SaO2. This measure was then not normally distributed and not sensitive enough to demonstrate a relationship with LV diastolic dysfunction.

How can we explain this relationship between OSA and LV diastolic function? First, the BP increase during OSA leads to a pressure overload inside the LV which in turn

causes filling impairment. Second, during apneas, there is an increase in sympathetic nervous system activity which can also cause LV pressure overload [7]. Moreover, after each microarousal, there is an increase in the pulmonary capillary wedge pressure, which can lead to a concomitant reduction in LV compliance. Another mechanism that can promote LV diastolic dysfunction is the greater frequency of episodes of negative intrathoracic pressure in apneic subjects. This pressure modification can lead to an increase in LV wall tension and LV afterload, culminating in a reduction in stroke volume during apneas. The overdistention of the right ventricle during OSA can also reduce LV filling. Increased arterial stiffness may also lead to LV diastolic dysfunction through an increase in LV systolic overload which can cause LVH and consequently changes to LV filling. Thus, some authors found a relationship between aortic stiffness and LV diastolic anomalies [13, 28]. This is partly confirmed by our data. Indeed, the significant negative relationship between the E/A ratio and PWV disappears when age and BP are taken into account. Another mechanism is a possible release of mediators affecting left ventricle due to the hypoxia-reoxygenation sequences. Indeed, in our study, the only parameter significantly associated with E/A ratio was mean nocturnal SaO2.

Left ventricular hypertrophy

Hypertension is the commonest risk factor for LVH and heart failure in longitudinal studies. LVH is a major and independent risk factor for cardiovascular events. In hypertensive patients, LVM has been found to be higher in non-dipper pattern subjects [29]. In our study, we did not found a similar result but 91% of the OSA patients with

LVH had nocturnal hypertension (vs. 67% in subjects without LVH). For these haemodynamic reasons, apneic patients are at greater risk of developing LVH.

The numerous episodes of hypoxaemia recorded during apneas also seem to play a role in the constitution of LVH. Another mechanism leading to LVH is the increased sympathetic activity observed during OSA. However, study results do not always point in the same direction. For some authors, LVH is more prevalent in OSA patients [30, 31]. In our study, we found a lower prevalence of LVH than the one observed in these previous studies. This can be explained in part by the characteristics of our population (ie newly diagnosed OSA patients without any known cardiovascular disease). Niroumand et al. concluded that OSA is not associated with increased LVM independently of obesity, hypertension, or advancing age [26].

It is not always possible to measure LVM in apneic patients as they are often overweight. Consequently, indexation of LVM to height$^{2.7}$ would seem to be more appropriate in apneic patients than indexation to BSA [21]. In our study, LVMI was significantly higher when there was a LV diastolic dysfunction when normalization for height$^{2.7}$ was used. In line with other authors, we found a positive and independent relationship between the severity of OSA, estimated by mean nocturnal SaO2, and LVM [11, 14, 32]. Conversely, Hedner et al. did not note such a link [30]. However, in their study, 17 of the 31 hypertensive patients were using pharmacological antihypertensive treatment.

Conclusion

LV diastolic dysfunction and LVH appear early in OSA patients, independently of their BP levels. This may partly explain the high prevalence of cardiovascular events

observed in this specific population. We found that only mean nocturnal SaO2 is associated with LV diastolic dysfunction and LVH. Given the cardiovascular risk associated with these cardiac anomalies, carrying out a cardiac Doppler ultrasound could be useful in the initial assessment of patients suffering from OSA.

Perspectives

Interventional studies are desirable in this field. The Arias et al.' randomized clinical trial in a small number of patients suggested that effective CPAP application led to LV diastolic function improvement [12]. In the current cohort, there is an on going study looking at CPAP efficacy on LV diastolic function.

Study limitations

The mitral flow velocity pattern has a limited ability to differentiate normal vs abnormal LV diastolic function due to the effects of loading conditions, age and HR. However, the parameters used in the present study have been validated by numerous studies and recommended in the recent ESH-ESC guidelines on hypertension [16].

We have used simplified techniques for assessing OSA diagnosis and severity in a subgroup of the included patients. However, diastolic dysfunction in our study mainly correlated with SaO2 parameters which are properly assessed by simplified sleep studies.

We acknowledge that the absence of a control group could be considered as an important study limitation. However, this lack of control group does not preclude the demonstration of an independent relationship between LV diastolic function and LVM on the one hand and mean nocturnal SaO2 on the other hand.

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Figure Legends

Figure 1. Mean nocturnal oxygen saturation was significantly lower in the abnormal diastole group (n=34) compared with the normal diastole group (n=116). Boxes represent values within the interquartile range; whiskers represent the data range; and the line across the boxes represents median values. SaO2 indicates oxygen saturation.

Figure 1.

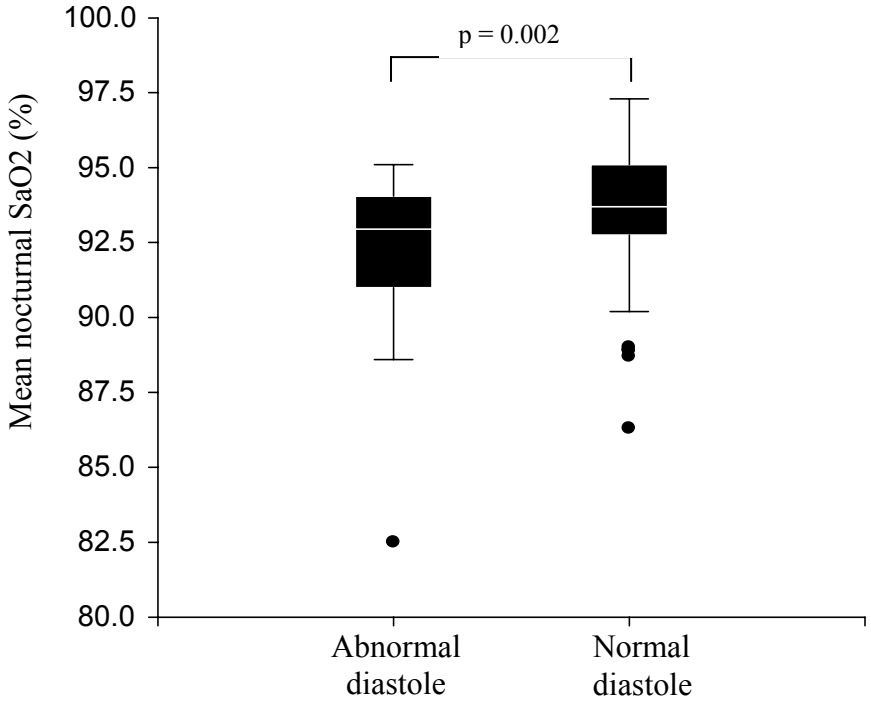
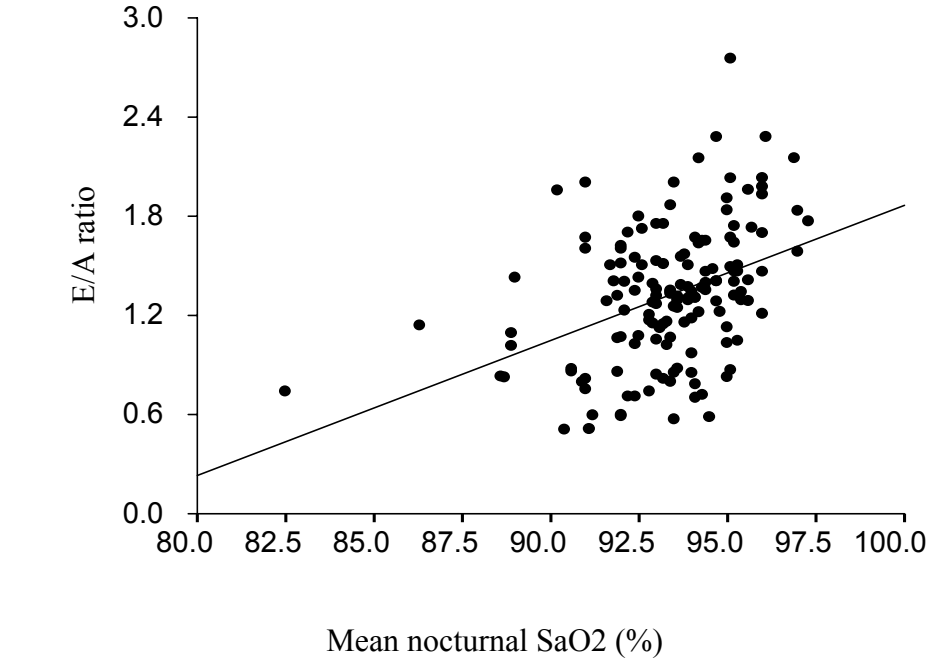


Figure 2. E/A ratio (top) and left ventricular mass index-height$^{2.7}$ (bottom) were correlated to mean nocturnal oxygen saturation (r=0.41, p<0.001 and r=-0.30, p=0.001 respectively). LVMI indicates the left ventricular mass index; SaO2 indicates oxygen saturation.

Figure 2.



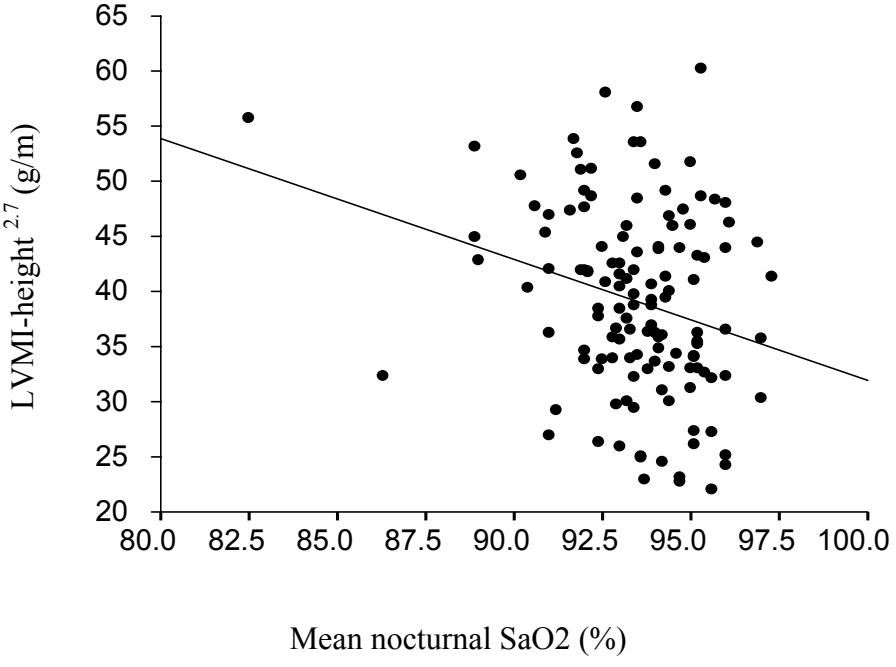


Table 1 Anthropometric, biological and haemodynamic characteristics of the OSA patients

	Global population (n=150)	Normal diastole (n=116)	Abnormal diastole (n=34)	p Value
Anthropometric and biological parameters				
Age (years)	49±11	46±10	57±9	**<0.001**
Male/female (n)	123/27	97/19	26/8	0.34
BMI (kg/m²)	27.1±3.3	27.0±3.2	27.6±3.5	0.36
Past or current smoking (%)	48	44.8	58.8	0.15
Total cholesterol (mmol/L)	5.39±1.11	5.34±1.08	5.52±1.19	0.28
Triglycerides (mmol/L)	1.37±1.11	1.36±1.13	1.44±1.02	0.69
HDL-cholesterol (mmol/L)	1.47±0.39	1.47±0.39	1.52±0.36	0.19
LDL-cholesterol (mmol/L)	3.30±0.98	3.30±1.0	3.50±0.93	0.38
Glucose (mmol/L)	5.08±0.76	5.06±0.68	5.12±0.98	0.30
Creatinine (µmol/L)	89.2±14.2	89.3±14.4	88.8±13.8	0.86
BP (mmHg) and HR parameters				
Clinic SBP	133±18	130±16	141±20	**<0.001**
Clinic DBP	87±11	85±10	92±11	**<0.001**
Clinic PP	46±11	45±11	50±12	**0.034**
Clinic HR, bpm	65±10	64±10	69±10	**0.012**
Daytime SBP	128±14	127±14	130±15	0.22
Daytime DBP	84±8	84±8	86±8	0.16
Daytime PP	44±9	43±9	44±10	0.53
Daytime HR, bpm	80±10	80±10	83±10	0.14
Nocturnal SBP	113±13	112±13	114±14	0.38
Nocturnal DBP	73±8	72±8	74±8	0.11
Nocturnal PP	40±9	40±9	40±10	0.83
Nocturnal HR, bpm	68±9	67±9	69±9	0.13
Non-dipper SBP, %	39	38	41	0.78
Non-dipper DBP, %	27	24	37	0.14
Non-dipper SBP and DBP, %	44	48	63	0.41

Data are expressed as mean (SD), unless otherwise stated. BMI, body mass index; BP, blood pressure; HR, heart rate; PP, pulse pressure.

Table 2 Respiratory, cardiac and arterial characteristics of the OSA patients

	Global population (n=150)	**Normal diastole** (n=116)	**Abnormal diastole** (n=34)	**p Value**
Sleep respiratory variables				
RDI, n/h	41±18	40.2±18.0	44.0±18.1	0.28
Microarousal index, n/h	37.2±14.7	37.2±14.7	37±14.9	0.94
Mean nocturnal SaO2, %	93.4±2.0	93.7±1.8	92.3±2.4	**0.002**
Minimal nocturnal SaO2, %	83.7±6.7	84.2±6.6	82.1±7.2	0.11
Percentage of recording time spent at a SaO2 <90%, %	7.3±15.8	6.1±14.9	11.4±18.2	0.13
Cardiac parameters				
IVS thickness, mm	8.5±1.2	8.4±1.2	8.9±1.4	0.06
LVPW thickness (mm)	9.0±1.2	8.9±1.1	9.4±1.3	0.055
LVD (mm)	48.7±4.8	48.7±4.8	48.4±4.9	0.75
LV systolic ejection volume (ml)	64.9±14.4	64.9±14.8	64.6±13.1	0.92
LVEF (%)	58±6	57.8±6.5	58.6±6.1	0.55
LVM (g)	170.1±42.4	167.7±41.4	179.1±45.5	0.21
LVMI-BSA (g/m²)	88.1±18.7	86.5±18.6	93.7±18.4	0.07
LVMI-height$^{2.7}$ (g/m)	39.1±8.4	38.2±8.3	42.5±8.3	**0.016**
LVH-BSA (%)	7.7	5.3	16.1	0.13
LVH-height$^{2.7}$ (%)	11.4	8.6	21.4	0.13
Left atrial diameter (mm)	35.7±4.7	35.7±4.6	35.9±4.9	0.82
E wave (m/s)	68±16	50.4±12.5	68.3±13.2	**<0.001**
A wave (m/s)	54±15	71.3±14.2	56.1±14.9	**<0.001**
E/A ratio	1.33±0.42	1.46±0.33	0.86±0.33	**<0.001**
Abnormal diastole (%)	23	0	100	**<0.001**
Arterial parameter				
Aortic PWV (m/s, N=124)	9.0±1.4	8.79±1.29	9.85±1.68	**0.001**

Data are expressed as mean (SD), unless otherwise stated. BSA, body surface area; IVS, interventricular septum; LV, left ventricular; LVD, left ventricular internal end-diastolic; LVEF, left ventricular ejection fraction; LVH, left ventricular hypertrophy;

LVM, left ventricular mass; LVMI, left ventricular mass index; LVPW, left ventricular posterior wall; PWV, pulse wave velocity; RDI, respiratory disturbance index; SaO2, oxygen saturation.