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Impact of the obstructive sleep apnea syndrome on left ventricular remodeling among people with different body weight

Ya. O. Andreieva, O. I. Tokarenko

SI "Zaporizhzhia Medical Academy of Post-Graduate Education Ministry of Health of Ukraine"

Key words: obstructive sleep apnea syndrome, left ventricular hypertrophy, cardiac remodeling, ventricular, obesity.

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E-mail: andryana08@gmail.com

The aim of the study: to estimate the structural changes of LV among people with unrecognized OSAS and different body weight.

Materials and methods. The study involved 74 patients with OSAS. All subjects were divided into two groups: with obesity and with normal body weight. Patients with hypertension, diabetes mellitus or any other known cardiac and renal diseases, with central sleep apnea were excluded from the study. 20 healthy people were included in the control group. Each patient underwent a clinical evaluation, 24-hour ambulatory blood pressure monitoring, cardiorespiratory monitoring, transthoracic echocardiography. Pearson correlation analysis, univariate and multivariate regression analysis were performed.

Results. Ten patients from all enrolled subjects were diagnosed with LV hypertrophy. Estimated LVM and LVMI increased in group I in comparison with the group II and control group. Significant differences between group II and control group concerning LVMI and LVM weren`t admitted. A significant difference for PWT_d and IVS_d were observed in group I and group II, compare to control group. The LVMI was positive ly correlated with DI even after adjustment for the BMI. The LVM correlate with mean SaO_2 and the lowest SaO_2. The univariate regression analysis showed that the lowest SaO_2, DI, AHI were associated with LVMI.

Conclusions. OSAS and obesity are associated with high LVM, LVMI and prevalence of concentric LV remodeling. The LVMI was increased parallel to an increasing in the OSAS severity in patients with obesity. There were admitted statistically significant differences for PWT_d and IVS_d among patients with OSAS without obesity and healthy people. Concerning LVMI and LVM, no statistically significant differences were admitted. The lowest SaO_2 and DI were associated with changes of LVMI, LVM, PWT_d and IVS_d according to the results of regression analysis.

Ключові слова: синдром обструктивного апное сну, гіпертрофія лівого шлуночка, ремоделювання серця, ожиріння.

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Вплив синдрому обструктивного апное сну на ремоделювання лівого шлуночка в пацієнтів із різною вагою тіла

Я. О. Андреєва, О. І. Токаренко

Мета роботи – оцінити структурні зміни ЛШ в осіб із недіагностованим СОАС і різною вагою тіла.

Матеріали та методи. У дослідженні взяли участь 74 пацієнти з СОАС. Усіх пацієнтів поділили на дві групи: з ожирінням і нормальною вагою тіла. Пацієнти з артеріальною гіпертензією, цукровим діабетом або будь-якими іншими кардіальними та нефрологічними захворюваннями, з центральним апное сну були виключені з дослідження. 20 здорових добровольців включені в контрольну групу. Кожен пацієнт мав клінічне обстеження, добовий моніторинг артеріального тиску, кардіо-респіраторний моніторинг, трансторакальну ехокардіографію. Проводився кореляційний аналіз, одно- і багатофакторний регресійний аналізи.

Результати. У 10 пацієнтів діагностована гіпертрофія ЛШ. ММЛШ і ІММЛШ була більшою у групі І порівняно з групою ІІ та контрольною групою. Вірогідні відмінності між групою ІІ та контрольною групою щодо ІММЛШ і ММЛШ не встановлені. Вірогідна різниця показників ТЗСЛШ і ТМШП спостерігалась у групі І і групі ІІ порівняно з контрольною групою. ІММЛШ позитивно корелював із ДІ. Не встановили статистично значущих кореляцій між ІММЛШ та ІАГ. ММЛШ позитивно корелювала з середнім SaO_2 та мінімальною SaO_2. Однофакторний регресійний аналіз показав, що мінімальна SaO_2, ДІ, ІАГ пов'язані з ІММЛШ.

Висновки. СОАС та ожиріння асоціюються з більшою ММЛШ, ІММЛШ і поширеністю концентричного ремоделювання ЛШ. ІММЛШ збільшувався паралельно зростанню тяжкості СОАС у пацієнтів з ожирінням. Встановили статистично значущі відмінності показників ТЗСЛШ і ТМЖП між групами пацієнтів із СОАС без ожиріння та здорових осіб. Щодо ІММЛШ і ММЛШ, статистично значущі відмінності не встановлені в цих пацієнтів. Мінімальний SaO_2 та ДІ пов'язані зі змінами ІММЛШ, ММЛШ, ТЗСЛШ і ТМЖП за результатами регресійного аналізу.

Ключевые слова: синдром обструктивного апноэ сна, гипертрофия левого желудочка, ремоделирование сердца, ожирение.

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Влияние синдрома обструктивного апноэ сна на ремоделирование левого желудочка у пациентов с разной массой тела

Я. А. Андреева, А. И. Токаренко

Цель работы – оценить структурные изменения ЛЖ сердца у пациентов с недиагностированным ОСАС и разной массой тела.

Материалы и методы. В исследовании приняли участие 74 пациента. Всех пациентов разделили на две группы: с ожирением и с нормальной массой тела. Пациенты с артериальной гипертензией, сахарным диабетом или другими кардиальными и нефрологическими заболеваниями, с центральным апноэ во сне исключены из исследования. 20 здоровых добровольцев включены в контрольную группу. Каждый пациент проходил клинико-лабораторное обследова-

ние, ЭКГ, суточное мониторирование артериального давления, кардио-респираторный мониторинг, трансторакальную эхокардиографию. Проводился корреляционный анализ, однофакторный и многофакторный регрессионный анализы.

Результаты. У 10 пациентов диагностирована гипертрофия ЛЖ. ММЛЖ и ИММЛЖ выше в группе I по сравнению с группой II и контрольной группой. Достоверные различия между группой II и контрольной группой по ИММЛЖ и ММЛШ не установлены. Достоверная разница для ТЗСЛШ и ТМШП наблюдалась в группе I и группе II по сравнению с контрольной группой. ИММЛЖ положительно коррелировал с СИ. Не установлено никаких статистически значимых корреляций между ИММЛЖ и ИАГ. ММЛШ положительно коррелировала со средней SaO_2 и минимальной SaO_2. Однофакторный регрессионный анализ показал, что минимальная SaO_2, ДИ, ИАГ связаны с ИММЛЖ.

Выводы. ОСАС и ожирение ассоциируются с большей ММЛЖ, ИММЛЖ и частотой встречаемости концентрического ремоделирования ЛЖ. ИММЛЖ возрастает с увеличением степени тяжести ОСАС у пациентов с ожирением. Установлены статистически значимые различия для ТЗСЛЖ и ТМЖП среди пациентов с ОСАС без ожирения и здоровых людей. Что касается ИММЛЖ и ММЛЖ, никаких статистически значимых различий в этой группе не установлено. Минимальная SaO_2 и СИ связаны с изменениями ММЛЖ, ИММЛЖ, ТЗСЛЖ и ТМЖП в соответствии с результатами регрессионного анализа.

Obstructive sleep apnea syndrome (OSAS) characterized by recurrent episodes of complete or partial obstruction of the upper airway during sleep, has widely gained interest since its initial description more than 40 years ago [1]. OSAS is associated with hypertension, insulin resistance, atrial fibrillation, stroke, and increased cardiovascular disease (CVD) morbidity and mortality. Disruption of sleep leads to increased sympathetic activation, metabolic changes, vasoconstriction, acute tachycardia, acute blood pressure elevation that results in increased left ventricular (LV) after load [1].

Left ventricular hypertrophy (LVH) is one of the well-knowing CVD risk factors and of ten associate with OSAS [2]. However, how OSAS impacts on left ventricular remodeling isn`t completely clear. On the one hand, LVH could be as a result of the OSAS itself. Some studies have shown that LVH is a common complication of OSAS and even without the potential cardiovascular disease, left ventricular systolic and diastolic dysfunction (LVSD and LVDD) and LVH were associated with OSAS. LVMI strongly correlate with OSAS severity and prevalence of LVH among patients with severe OSAS is high [3]. But other authors claim that LHV could be caused by the OSAS comorbidities such as hypertension, obesity and metabolic deregulations, and the LVMI differ significantly only between the patients with the OSAS who suffer from hypertension, obesity, and/or diabetes mellitus [2]. Furthermore, obesity is an additional risk factor for development of LVH and increasing of CVD risk.

Purpose

The aim of the current study is to estimate the structural changes of LV among people with unrecognized OSAS and different body weight.

Materials and methods

Subjects of this study were recruited from 418 consecutive adults with OSAS who underwent overnight cardiorespiratory monitoring between November 2011 and August 2016. All subjects didn`t have previous treatment of OSAS. Our present research was approved by the clinical research ethic committee of SI "Zaporizhzhia Medical Academy of Post-Graduate Education Ministry of Health of Ukraine". Written informed consent was obtained from all patients.

Each patient underwent a clinic ale valuation during consultation, biological tests, electrocardiogram (Cardio Sens, XAI-Medica, Ukraine), 24-hour ambulatory blood pressure monitoring (ABPM–04, Meditech, Hungry). Hypertension was defined as blood pressure ≥125/80 mmHg during ABP M and/or use of antihypertensive medication. When first stage of investigation was completed, patients with hypertension, diabetes mellitus or any other known cardiac and renal diseases, with central sleep apnea were excluded from the study. Finally, 74 (52 men and 22 woman) eligible patients were enrolled. All these patients underwent transthoracic echocardiography. Body mass index (BMI) of the patients were calculated as weight divided by height square ($kg \cdot m^2$). According to BMI, all subjects were divided in to two groups. The first group includes participants with obesity (BMI ≥30 $kg \cdot m^2$) (46 subjects), the second group – with normal body weight (28 subjects). Twenty two healthy people were included in the control group. The mean age and gender were similar between the groups.

Cardiorespiratory monitoring was conducted for OSAS diagnosis by Somno check 2.0 (Weinmann, Germany). The apnea-hypopnea index (AHI) was defined as the number of apneas and hypopnea as per hour of sleep. According to the American association of sleep medicine [4], the severity of OSAS was classified as mild (5≤ AHI <15 events/hour), moderate (15≤ AHI ≤30 events/hour) and severe (AHI >30 events/hour). Desaturation index (DI) was defined as the percentage of sleep time with oxygen saturation <90 %. Clinical characteristic of enrolled patients are shown in *Table 1.*

Transthoracic echocardiography was performed with Siemens ACUSON X300 ultrasound machines, with a 1.75 MHz probe. Basic measurements of LV dimensions in diastole and systole, thicknesses of inter ventricular septum (IVS_d) and left ventricular posterior wall (PWT_d), and left ventricular mass (LVM) was measured by the M-mode technique according to European Association of Cardiovascular Imaging [5]. The left ventricular mass index (LVMI) was calculated. LVH was defined as LVMI ≥125 g/m^2. LV geometry was categoryzed into 4 groups: normal structure (LVMI <125 g/m^2 and RWT <0.45), eccentric hypertrophy (EH, LVMI ≥125 g/m^2 and RWT <0.45), concentric remodeling CR, LVMI <125 g/m^2 and RWT ≥0.45), and concentric hypertrophy (LVMI ≥125 g/m^2 and RWT ≥0.45).

Statistical analysis. The quantitative variables were expressed as means ± SD. Categorical variables were presented as percentages. The differences in each variable were evaluated by the Student's *t*-test for continuous variables and the χ^2 test for categorical variables. The relationships between parameters were evaluated by Pearson correlation analysis and univariate regression analysis. Multivariate

Table 1. Clinical characteristic of enrolled patients

Parameters, units	Group 1 (n = 46)	Group 2 (n = 28)	Group 3 (n = 22)	P
Male/Female (n)	33/13	20/8	14/8	N/A
Mean age (years)	36.5 ± 6.8	41.6 ± 7.2	36.8 ± 6.7	P_{1-3} – 0.093 P_{1-2} – 0.072 P_{2-3} – 0.066
BMI (kg/m^2)	33.2 ± 4.3	23.5 ± 3.6	23.1 ± 3.3	P_{1-3} – 0.009 P_{1-2} – 0.008 P_{2-3} – 0.063
SBP (mmHg)	128.3 ± 10.6	118.2 ± 7.7	112.3 ± 6.9	P_{1-3} – 0.063 P_{1-2} – 0.069 P_{2-3} – 0.092
DBP (mmHg)	79.4 ± 9.3	72.9 ± 6.5	73.1 ± 6.2	P_{1-3} – 0.059 P_{1-2} – 0.077 P_{2-3} – 0.068
AHI (events/per hour)	21.3 ± 4.1	18.2 ± 3.3	2.5 ± 1.0	P_{1-3} – 0.003 P_{1-2} – 0.071 P_{2-3} – 0.010
Mild OSAS (n)	20	11	0	N/A
Moderate OSAS (n)	21	11	0	N/A
Severe OSAS (n)	13	6	0	N/A
DI (per/hour)	22.6 ± 5.8	13.5 ± 5.4	1.1 ± 0.4	P_{1-3} – 0.009 P_{1-2} – 0.030 P_{2-3} – 0.013
Minimum SaO_2 (%)	82.3 ± 6.4	87.4 ± 4.5	97.4 ± 1.5	P_{1-3} – 0.022 P_{1-2} – 0.042 P_{2-3} – 0.011
Mean SaO_2 (%)	92.9 ± 5.6	95.5 ± 3.2	98.3 ± 1.2	P_{1-3} – 0.004 P_{1-2} – 0.051 P_{2-3} – 0.048
Sleep duration (%)	6.2 ± 4.2	5.5 ± 2.7	6.9 ± 1.1	P_{1-3} – 0.059 P_{1-2} – 0.066 P_{2-3} – 0.052

Table 2. Echocardiographic measures in obtained patients

Parameters, units	Group 1 (n = 46)	Group 2 (n = 28)	Group 3 (n = 22)	P
LA, cm	2.74 ± 0.38	2.72 ± 0.41	2.66 ± 0.23	P_{1-3} – 0.088 P_{2-3} – 0.074
LVM, gr	189.7 ± 35.15	141.3 ± 23.2	127.56 ± 21.74	P_{1-3} – 0.013 P_{2-3} – 0.058
LVMI, gr/m^2	92.11 ± 28.15	71.66 ± 15.90	61.14 ± 11.28	P_{1-3} – 0.008 P_{2-3} – 0.066
PWT_d, sm	1.11 ± 0.14	0.93 ± 0.17	0.79 ± 0.12	P_{1-3} – 0.024 P_{2-3} – 0.074
IVS_d, sm	1.13 ± 0.15	0.86 ± 0.17	0.76 ± 0.13	P_{1-3} – 0.028 P_{2-3} – 0.018

logistic regression analysis using statistically significant variables from the univariate analysis was performed to identify variables that were independently associated with LVH. A P value <0.05 was considered to indicate a statistically significant difference between groups. Calculations were performed using SPSS-software (Version 13.0; SPSS, Chicago, IL).

Results and discussions

The demographic, cardio-monitoring and echocardiographic parameters were compared between the groups. Echocardiographic measures in obtained patients.

Estimated LVM was increased in group I in comparison with the group II and control group (268.7 ± 65.15; 161.3 ± 43.2; 127.56 ± 21.74 respectively, P = 0.008; 0.005). LVMI (g/m) was also significantly increased in patients with obesity and OSA (47 ± 1.8 vs. 40 ± 1.5, P < 0.01). Significant differences between group II and control group concerning LVMI and LVM weren`t admitted. The LVMI was increased parallel to an increase in the OSAS severity in the groups I and II, but that increasing failed to constitute statistical significance in group II (P = 0.095).

Ten patients from all enrolled subjects were diagnosed with LV hypertrophy. Nine (90 %) of these patients were in group I. All these patients had severe OSAS (AHI, (36.55 ± 8.41) e/h). Concentric remodeling was diagnosed in 9 patients (8 patients from group I and 1 patient from group II) and concentric hypertrophy was observed in one patient. In comparison with group without LVH patients with diagnosed LVH have higher level of AHI (38.2 ± 17.8 vs. 24.6 ± 13.3) and DI (6.3 ± 3.2 Vs.18.6 ± 8.8) (P = 0.011).

Statistically significant positive correlations were detected between the BMI and cardio-respiratory parameters-the AHI, mean SaO_2, the lowest SaO_2, and DI SaO_2 <90 % (r = 0.232; P = 0.003; r = 0.44; P = 0.010; r = 0.28; P = 0.01; and r = 0.38; P = 0.007 respectively). The LVMI was positively correlated with DI (r = 0.74, P = 0.011) even after adjustment for the BMI (r = 0.27; P value = 0.042). There were no statistically significant correlations between the LVMI and the AHI (r = 0.16, P = 0.082). The LVM correlate with mean SaO_2 (r = -0.22, P = 0.06), and the lowest SaO_2 (r = -0.18, P = 0.06). Positive significant correlation was detected between PWT_d and DI (r = 0.35, P = 0.001) and non-significant correlation was detected between IVS_d and AHI (r = -0.26; P = 0.072). The univariate regression analysis showed that the lowest SaO_2, DI, AHI were associated with LVMI. Multivariate regression analyses adjusted for age, gender, BMI, the lowest SaO_2, mean SaO_2, AHI and DI were performed to assess the contribution of the variables in LV changes. A 1 % decrease in the lowest SaO_2 saturation was associated with a LVMI increase of 2.5 gr (P = 0.02), increase in IVS_d of 0.08 cm (P < 0.05) and an increase in PWT_d thickness of 0.03 cm. An increase DI in 1 % lead to increasing of LVMI of 2.6 gr and PWT_d thickness of 0.05 cm.

The results of our analysis highlight the importance of hypoxia severity, not just the AHI, in promoting cardiac remodeling. Results of our study have confirmed in some studies. The Wisconsin Sleep Cohort Study [6] showed a significant association with baseline AHI severity and LVH, but relationships became non-significant when BMI was added to the model. Mean SaO_2 and DI were independent predictors of LVM and LVMI in adjusted logistic regression models in this study. In our study we confirm a stronger correlation for DI than for AHI. We didn't obtain significant difference for mean SaO_2 for all participants of our study and differences were significant only for patients with severe OSAS. Furthermore, in the study of Seyed Hashem Sezavar et al. [7]. LV hypertrophy not only occurred more frequently in those with severe OSAS (66 %), but an increase in the LVMI was strongly correlated with arise in the DI even after adjustment for the BMI. All patients with LVH in our study have severe OSAS. But hypertension patients didn't exclude from these studies [7] and that fact could influence the results.

Our study has several limitations. Our study was across-sectional study, and included small amount of subjects, that could distort results. The study included considerably fewer female patients and patients older 65 years meeting our criteria, that also could influence study`s results.

Conclusions

1. OSAS and obesity are associated with high LVM, LVMI and prevalence of concentric LV remodeling. The LVM and LVMI were increased parallel to an increasing in the OSAS`s severity in patients with obesity.

2. There were admitted statistically significant differences for PWT_d and IVS_d among patients with OSAS without obesity and healthy people. Concerning LVMI and LVM, no statistically significant differences were admitted.

3. The lowest SaO_2, DI, BMI were associated with changes of LVMI, LVM, PWT_d and IVS_d according to the results of regression analysis.

Prospects for further research. It is planned to study the changes of the structural and functional parameters of the heart among patients with OSAS, hypertension, diabetes, establish their prognostic role in LVH against the background of overweight and obesity.

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Information about authors:
Andreieva Ya. O., MD, PhD, Associate Professor, Department of therapy, physiotherapy, resort therapy and occupational medicine of the SI "Zaporizhzhia Medical Academy of Post-Graduate Education Ministry of Health of Ukraine".
Tokarenko O. I., MD, PhD, DSci, Professor, Head of the Department of therapy, physiotherapy, resort therapy and occupational medicine of the SI "Zaporizhzhia Medical Academy of Post-Graduate Education Ministry of Health of Ukraine".

Відомості про авторів:
Андреєва Я. О., канд. мед. наук, доцент каф. терапії, фізіотерапії, курортології і профпатології, ДЗ «Запорізька медична академія післядипломної освіти МОЗ України».
Токаренко О. І., д-р мед. наук, професор, зав. каф. терапії, фізіотерапії, курортології і профпатології, ДЗ «Запорізька медична академія післядипломної освіти МОЗ України».

Сведения об авторах:
Андреева Я. А., канд. мед. наук, доцент каф. терапии, физиотерапии, курортологии и профпатологии, ГУ «Запорожская медицинская академия последипломного образования МЗ Украины».
Токаренко А. И., д-р мед. наук, профессор, зав. каф. терапии, физиотерапии, курортологии и профпатологии, ГУ «Запорожская медицинская академия последипломного образования МЗ Украины».

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