

# Relationship between Pulmonary Artery Diameter and Pulmonary to Aortic Artery Diameter Ratio in High Risk Individuals for Obstructive Sleep Apnea without Pulmonary Artery Hypertension Based on the Berlin Questionnaire

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**Background:** A significant association has been found between the pulmonary artery (PA) diameter and obstructive sleep apnea (OSA) in patients with pulmonary artery hypertension (PAH). We aimed to evaluate the relationship between the diameters of the PA trunk and aortic artery with their ratio as PAH markers in high risk cases for OSA based on the Berlin questionnaire without PAH.

**Materials and Methods:** This case-control study included 161 non-PAH patients admitted to a multi-slice CT scan ward. Filling out the Berlin questionnaire, the patients were divided into high and low risk cases for OSA. The diameters of the PA trunk and aortic ascending aorta and their ratio were assessed using the multi-slice CT scan.

**Results:** The PA to aortic ratios in the case and control groups were  $0.89\pm 0.17$  and  $0.88\pm 0.17$ , respectively, which all were non-significant. With regard to gender, the PA diameter was significantly lower among males in the control group than in the case group ( $P=0.034$ ). The mean PA to aortic ratio was slightly higher but statistically non-significant in the case group than in the control group. The aortic diameter showed a statistically significant increase by age in the case group ( $r=0.374$ ,  $P=0.003$ ) compared to the other group. However, the PA diameter increased significantly by age in both groups ( $r=0.184$ ,  $P=0.020$ ).

**Conclusion:** The PA diameter can be considered as a predicting factor for future cardiovascular diseases in high risk males for OSA based on the Berlin questionnaire without PAH. More studies are required to confirm these findings.

**Key words:** Obstructive sleep apnea; Berlin questionnaire, diameter of pulmonary artery trunk; multi-slice CT scan

## INTRODUCTION

The early diagnosis and treatment of obstructive sleep apnea (OSA) are essential for the prevention of cardiovascular diseases (CVDs) (1). The definitive diagnosis of OSA is based on polysomnography. However,

this method is cumbersome, time consuming, and expensive and also requires an equipped laboratory and trained personnel for the exact interpretation of data. Thus, most of apnoeic cases remain undiagnosed and untreated throughout their life. Various diagnostic tools have been

developed for the early diagnosis of this disease such as the Berlin, Stop, and Stop-Bang questionnaires (2). The termination of apnea and hypopnea episodes is associated with CNS arousal, which is manifested by sleep fragmentation and major cardiovascular squeals as an abrupt increase in the heart rate and blood pressure (3). The high prevalence of pulmonary artery hypertension (PAH) has been observed in cases with OSA and daily hypoxia is the main determinant (4). Nocturnal hypoxia is not the sole reason for the PAH pathogenesis in cases with OSA and pulmonary hemodynamic consequences of sleep apnea are the current focus of research.

Pulmonary artery (PA) dilatation is an index of increased PA pressure (5). Increased PA dilatation has been observed in cases with OSA with PAH (6). The PA diameter has not been evaluated in OSA cases without PAH. Since PA dilatation is an index of PAH, we aimed to evaluate the relationship between the PA trunk diameter and high risk cases for OSA based on the Berlin questionnaire without PAH and the PA trunk diameter. Several investigations have used the PA diameter and its ratio to the ascending aorta diameter as an indicator for the determination of PAH (7).

The association of the PA diameter with OSA was studied previously in PAH patients. In this study, we aimed to investigate this association in high risk cases for OSA based on the Berlin questionnaire without PAH patients.

## MATERIALS AND METHODS

The Berlin questionnaire was completed by 161 adults who were asked to perform multidetector CT (MDCT) after obtaining their signed informed consent. The participants were selected using simple random sampling. The exclusion criteria were patients with chronic obstructive pulmonary disease, PAH, and valvular heart disease. Demographic data were collected. Height, weight, body mass index (BMI), and systolic and diastolic blood pressure were also measured. Based on scores derived from the Berlin questionnaire, 62 and 98 low and high risk cases for

OSA without PAH were categorized as cases and controls, respectively. The Berlin questionnaire is one of the most valid questionnaires for risk stratification in sleep apnea with 86% sensitivity and 77% specificity (8). Then, CT angiography was performed for all the participants using 64 MDCT. The PA diameter was measured at bifurcation level using 4.3 ADW reporting system software. Simultaneously, the ascending aorta diameter was measured and the pulmonary to aortic radius ratio was calculated. The study was approved by the Institutional Review Board and Ethics Committee of Islamic Azad University, Najafabad Branch.

### Statistical analysis

The results were presented as mean  $\pm$  standard deviation (SD) for quantitative variables and absolute frequencies and percentages for categorical variables. Crude effects were compared between the study groups using an independent samples t-test, while normality assumptions were held. The analysis of covariance (ANCOVA) was performed to compare the effect of apnea after adjusting for age, sex, and BMI. Pearson's correlation coefficient was used to determine the association between age with pulmonary and aortic diameters. All the analyses were performed using IBM SPSS for windows (version 22.0, SPSS Inc, Chicago, IL, USA). A P-value of 0.05 was considered as statistically significant.

## RESULTS

The mean age distribution of the 161 participants was  $54.2 \pm 12.2$  ( $55.9 \pm 11$  years old vs.  $53.1 \pm 12.9$  years in the case and control groups, respectively). Based on the Berlin questionnaire, 39% of the participants were diagnosed as high risk cases for OSA without PAH. Totally, 69.6% of the participants were male, although the gender difference was non-significant. The mean BMI was  $27.4 \pm 4.3$  and the mean diameters of ascending aorta and pulmonary trunk were  $3.2 \pm 0.5$  and  $2.8 \pm 0.5$  cm, respectively. The mean ratio of the PA trunk to the ascending aorta diameter was  $0.89 \pm 0.17$  (Table 1). These measures did not show any significant difference between the groups, even after adjustment for

age, gender, and BMI ( $P>0.05$ ) (Table 2). Regarding gender, the PA diameter was lower among males in the control group than in the case group and was statistically significant ( $P=0.034$ ) (Table 3).

Table 1. Basic characteristics in participants

Variables	Total
Gender (Male)	112(69.6)
Age (years)	54.2±12.2
Aortic artery diameter (cm)	3.2±0.5
Pulmonary artery diameter (cm)	2.8±0.5
Pulmonary/Aortic artery diameter ratio	0.89±.17
Body mass index (kg/m <sup>2</sup> )	27.4±4.3

Table 2. Effect of apnea on aortic and pulmonary artery and diameter ratio (crude and adjusted effects).

Parameter		Case group	Control group	P-Value
		(n=99)	(n=62)	
Aortic artery diameter	crude effect	0.52±3.2	0.63±3.3	0.350
	Model 1	0.58±3.2	0.61± 3.3	0.358
	Model 2	0.6±3.2	0.61± 3.3	0.664
Pulmonary artery diameter	crude effect	0.6±2.8	0.5±2.9	0.101
	Model 1	0.6±2.8	0.7±2.9	0.191
	Model 2	0.6±2.7	0.7±2.8	0.296
(Pulmonary/Aortic) artery diameter ratio	crude effect	0.17±0.88	0.17±0.89	0.567
	Model 1	0.19±0.87	0.19±0.89	0.541
	Model 2	0.18±0.87	0.20±0.89	0.407

Model 1: Age and gender adjustment, Model 2: Age, gender and BMI adjustment.

Table 3. Effect of apnea on aortic and pulmonary artery and diameter ratio based on sex

Parameter		Case group	Control group	P-Value
Aortic artery diameter	Female	0.43±3.28	0.56±3.16	0.406
	Male	0.73±3.48	0.51±3.28	0.429
Pulmonary artery diameter	Female	0.33±2.73	0.69±2.78	0.742
	Male	0.51±3.07	0.54±2.84	0.034
Ratio of pulmonary to aortic artery diameter	Female	0.14±0.85	0.22±0.89	0.492
	Male	0.18±0.93	0.15±0.87	0.099

There was no significant association between age and the PA trunk to the ascending aorta diameter ratio in the both groups. However, a statistically significant increase was observed in the PA trunk to the ascending aorta diameter ratio by age in the both groups. The PA trunk diameter was slightly larger but statistically non-

significant in the cases than in the controls. The aortic diameter showed a statistically significant increase by age in the case group ( $r=0.374$ ,  $P=0.003$ ) compared to the control group, while the PA diameter showed a significant increase by age in the both groups ( $r=0.184$ ,  $P=0.020$ ) (Table 3).

## DISCUSSION

The quantity and quality of sleep impact health status and have been recognized as fundamental determinants of the quality of life (9). Sleep breathing disorders such as OSA are very common and the early identification of them could have beneficial impact on health status (10). However, the early detection of these disorders is impossible in some circumstances. Thus, it might be fundamental to detect predisposing factors or risk determinants in this regard. We proposed that the PA diameter and the aortic to PA diameter ratio could be considered as risk determinants for OSA.

In the study, we found that men were at higher risk for OSA, which could justify more male referrals to CT angiography and a higher prevalence of coronary heart disease in men. Meuleman et al. showed that gender could strongly predict the ascending aorta diameter in patients at high risk for OSA. However, gender was not related to the PA trunk to the ascending aorta diameter ratio in our study (11). We did not find any significant difference between the case and control groups regarding gender, which is inconsistent with findings that showed gender as a risk factor for OSA. However, the relationship was significant between BMI and being at high risk for OSA, which is compatible with previous findings. The increase in the aortic artery diameter by age occurred only in cases at high risk for OSA. This finding is compatible with Meuleman et al.'s findings (11). Baguet et al. demonstrated an increased ascending aorta size in association with nocturnal hypoxia in cases at high risk for OSA due to the decreased baroreflex sensitivity and the increased diastolic blood pressure (12). Lee et al. demonstrated the detrimental impact of the increased afterload from systemic hypertension on aortic functional indices (13).

The main finding of our study is the lower PA diameter in high risk males for OSA compared to their low risk counterparts based on the Berlin questionnaire, all without PAH. The dilated PA has been demonstrated in OSA patients with resistant systemic hypertension (14). Sleep apnea is a common disorder and the development of PAH brings poor prognosis in patients. Thus, it is essential to develop new screening tools (15, 16). Since we excluded the presence of PAH, the increased PA diameter in males with OSA could be considered as a risk factor for the development of further CVDs such as PAH. The increased PA diameter was previously reported in various conditions with the increased PA pressure. However, to our knowledge, we for the first time reported the increased PA diameter in high risk cases for OSA based on the Berlin questionnaire but without PAH. Furthermore, we showed a higher PA diameter by age in the cases and the controls. This finding that was not reported before is not affected by the presence of OSA, as we observed it in the both groups. It is obvious from previous reports that systolic artery pressure increases by age. Since there are no reports similar to our results on the diameter of PA, we suggest further studies in this regard. The small sample size and not using polysomnography as a gold standard to confirm the diagnosis of sleep apnea were the main limitations of the study.

## CONCLUSION

The PA diameter was higher in high risk cases for OSA based on the Berlin questionnaire without PAH. Thus, the PA diameter can be considered as an early marker and a predicting factor for future CVDs in male cases with OSA. However, more studies are needed to confirm these findings.

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