https://doi.org/10.5664/jcsm.8770

JCSM | Journal of Clinical Sleep Medicine

SCIENTIFIC INVESTIGATIONS

Effects of obstructive sleep apnea on the thoracic aorta and the main pulmonary artery: assessment by CT

Roberto Castellana, MD[1]; Giacomo Aringhieri, MD[1]; Luna Gargani, MD, PhD[2]; Michelangelo Maestri, MD, PhD[3]; Alessandro Schirru, MD[3]; Enrica Bonanni, MD[3]; Ugo Faraguna, MD, PhD[4,5]

[1]Diagnostic and Interventional Radiology, University of Pisa, Pisa, Italy; [2]Institute of Clinical Physiology, National Research Council, Pisa, Italy; [3]Department of Clinical and Experimental Medicine, Neurology Unit, University of Pisa, Pisa, Italy; [4]Department of Translational Research and of New Surgical and Medical Technologies, University of Pisa, Pisa, Italy; [5]Department of Developmental Neuroscience, IRCCS Fondazione Stella Maris, Pisa, Italy

Study Objectives: The influence of obstructive sleep apnea (OSA) on thoracic aortic size is debated. We aimed to identify possible relations between sleep parameters and the sizes of the ascending aorta (AA), the descending thoracic aorta (DTA), and the main pulmonary artery (MPA) in patients with untreated OSA and in a subgroup of participants without comorbidities capable of affecting the size of great thoracic vessels.

Methods: We retrospectively measured AA, DTA, and MPA sizes on the chest computed tomography scans of 60 patients with OSA who underwent sleep studies within 1 year before or after the computed tomography. Univariate and multivariate analyses were performed on all patient findings, while an additional univariate analysis was conducted on the data for 22 participants without comorbidities. The latter had been divided into subgroups depending on the sleep parameters, and comparisons were made between them.

Results: The logarithm of the time of oxygen saturation below 90% (CT90) significantly predicted AA and MPA sizes in all patients with OSA ($P < .05$). Oxygen desaturation index and minimum oxygen saturation were moderately correlated with AA and DTA sizes in patients without comorbidities ($P < .01$). In this group, subjects with oxygen desaturation index > 30 or minimum oxygen saturation < 81% had greater AA and DTA dimensions ($P < .05$).

Conclusions: In patients with OSA, time of oxygen saturation < 90% influenced AA and MPA sizes. In those patients without comorbidities, oxygen desaturation index and minimum oxygen saturation were moderately correlated with both AA and DTA sizes. Participants without comorbidities with oxygen desaturation index > 30 or minimum oxygen saturation < 81% had greater AA and DTA dimensions.

Keywords: dilation, size, ascending aorta, descending aorta, main pulmonary artery, computed tomography

Citation: Castellana R, Aringhieri G, Gargani L, et al. Effects of obstructive sleep apnea on the thoracic aorta and the main pulmonary artery: assessment by CT. *J Clin Sleep Med*. 2021;17(1):3–11.

BRIEF SUMMARY

Current Knowledge/Study Rationale: Obstructive sleep apnea is associated with cardiovascular comorbidities, but its influence on the size of the thoracic aorta remains debated. No previous studies assessed the relation between obstructive sleep apnea and main pulmonary artery size.

Study Impact: In patients with obstructive sleep apnea, sleep variables associated with oxygen desaturation influence the size of the great thoracic vessels.

INTRODUCTION

Obstructive sleep apnea (OSA) is characterized by repeated episodes of complete or partial collapse of the upper airway during sleep, with consequent decrease in oxygen saturation and/or arousal. It is associated with an increased risk of cardiovascular comorbidities[1] but the impact on the thoracic aortic size is still rather controversial.[2]

Some speculations about the mechanisms through which OSA may promote aortic dilatation have been proposed. One hypothesis identifies intrathoracic pressure changes that take place during apneic episodes and during inspiratory efforts as the most relevant stretching trigger impinging on the aortic wall. In animals, the aortic dilatation during apnea has already been demonstrated[3,4]; in humans, experiments suggest the presence of a more negative intrathoracic pressure during apnea, compared to physiological respiration.[5] In addition, an increase in the proximal aortic diameter has been observed in healthy volunteers during simulated obstructive apnea.[6]

Another mechanism hypothesizes oxygen desaturation and, with a minor role, hypercapnia and central nervous system arousals as triggers for aortic dilation. In particular, during hypoxia, chemoreceptor stimulation leads to hyperventilation. This is followed by sustained daytime activation of the sympathetic nervous system,[7] which causes vasoconstriction and increment of blood pressure. Subsequent hypertension could lead to the increment of the aortic size.[8]

Another theoretical mechanism considers the inflammatory process as a potential cause of aortic dilation. Noninfectious inflammation of the ascending aorta (AA) is generally associated with atherosclerosis, giant cell arteritis, Takayasu arteritis, granulomatosis with polyangiitis, sarcoidosis, IgG4-related sclerosing disease–associated aortitis.[9] In patients with OSA, levels of serum inflammatory markers are higher compared to

control subjects.[10–12] Furthermore, expansion and activation of the macrophage population has been demonstrated in the aortic walls of mice exposed to intermittent hypoxia.[13] This inflammatory process could potentially lead to the formation of aortic aneurysms. Murine and in vitro models demonstrated that white adipose tissue could have a pivotal role as the source of proinflammatory mediators in response to intermittent hypoxia.[14]

A positive association between OSA severity and size of the AA has been previously reported[15–19]; however, these results were not consistent with findings of other authors.[20–23]

Methodological limitations and cohort study heterogeneity may have contributed to this discrepancy. In particular, the inclusion of patients in treatment for OSA, or with significant comorbidities, the use of different sleep variables and OSA definitions criteria, and the application of different anatomic landmarks for vascular measurement.

In addition, previous studies did not investigate the fact that the descending thoracic aorta (DTA) and the main pulmonary artery (MPA) may be influenced by OSA also, through the same mechanisms proposed for the AA. In fact, the high prevalence of pulmonary hypertension is a clue to the possible influence of OSA on the MPA.[24] Indeed, in patients with OSA, pulmonary hypertension is usually mild, but it may be severe in 33% of cases,[25] representing a potential risk factor for aneurysm development, as described in some case reports.

Taking into account these considerations, the aim of our study was to evaluate AA, DTA, and MPA dimensions, taking advantage of the computed tomography (CT) approach, both in patients with OSA and in a selected subgroup of participants without comorbidities.

METHODS

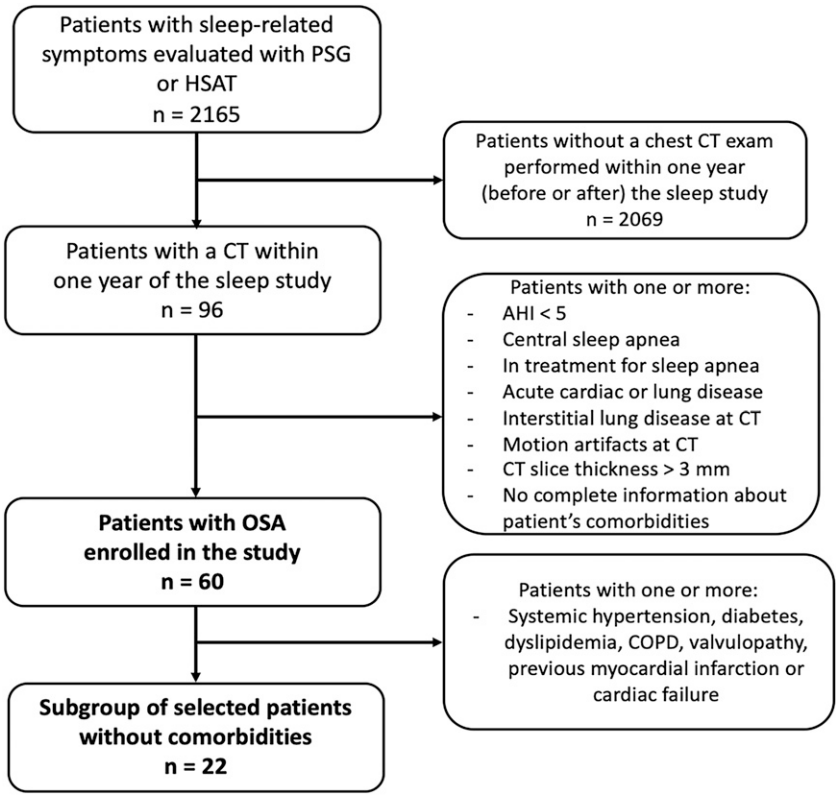
Study population

We conducted a retrospective study on a cohort of 60 patients with untreated OSA, including participants with nonacute cardiovascular and metabolic comorbidities (hypertension, type 2 diabetes, chronic obstructive pulmonary disease (COPD), and a history of myocardial infarction, valvular heart disease, and heart failure), and on a selected subgroup of 22 patients without any comorbidity.

The study initially included 2165 patients who were referred to the Pisa University Hospital Sleep Centre for a clinical evaluation of symptoms compatible with sleep breathing disorders, between January 2015 and July 2018. All patients underwent either polysomnography or home sleep apnea test.

Through our Picture Archiving and Communication System (Synapse, Fujifilm Medical Systems, Lexington, MA) we identified chest CT scans conducted on these patients, for clinical reasons other than OSA, within a year before or after the date of the sleep study. Ninety-six patients belonging to the sleep-breathing-disorders cohort met our search criteria. Sixty of these patients were selected after application of the following

Figure 1—Flow chart showing study cohort and adopted exclusion criteria.



COPD = chronic obstructive pulmonary disease, HSAT = home sleep apnea testing, OSA = obstructive sleep apnea, PSG = polysomnography.

exclusion criteria: apnea-hypopnea index (AHI) < 5 events/h, central sleep apnea, being under any type of treatment for sleep apnea at the time of both the sleep study and the chest CT exam, evident cardiac or pulmonary comorbidities at CT that could potentially influence vascular diameters (ie, pulmonary artery embolism, acute cardiac failure, pneumonia, interstitial lung disease), excessive motion artifacts at the site of measurement of the AA, absence of complete information about patient's comorbidities, CT slice reconstruction thickness > 3 mm.

The subgroup of patients without any history of comorbidities potentially influencing the vascular size (ie, systemic hypertension, diabetes, dyslipidemia, chronic obstructive pulmonary disease, history of myocardial infarction, valvular heart disease, or heart failure) was further investigated (**Figure 1**).

Characteristics of patients considered in the study were: age at the date of the sleep study, sex, body surface area (BSA), hypertension, type 2 diabetes, and COPD.

Written informed consent was obtained from patients; the study was performed in accordance with the ethical standard laid down in the 1964 Declaration of Helsinki and its later amendments.

Diagnosis of OSA

OSA was detected according to the third edition of *International Classification of Sleep Disorders*.[26] While 510 patients were tested with in-lab night-polysomnography, 1,655 patients underwent home sleep apnea tests, according to standard guidelines.[27] Sleep recordings were scored according to standard criteria,[28] and AHI, oxygen desaturation index (ODI), percentage of time of oxygen saturation < 90% (CT90), mean nocturnal oxygen saturation (mean SaO_2), and minimum nocturnal oxygen saturation (minimum SaO_2) were considered. SaO_2 recordings were visually reviewed to reject possible artifacts. In particular, an apnea was defined as an interruption of airflow for ≥ 10 seconds; while a respiratory event was scored as hypopnea when the following 3 criteria were all met: drop in the airflow ≥ 30% compared to pre-event baseline airflow, duration of the airflow drop ≥ 10 seconds, and a > 3% oxygen desaturation from pre-event baseline.

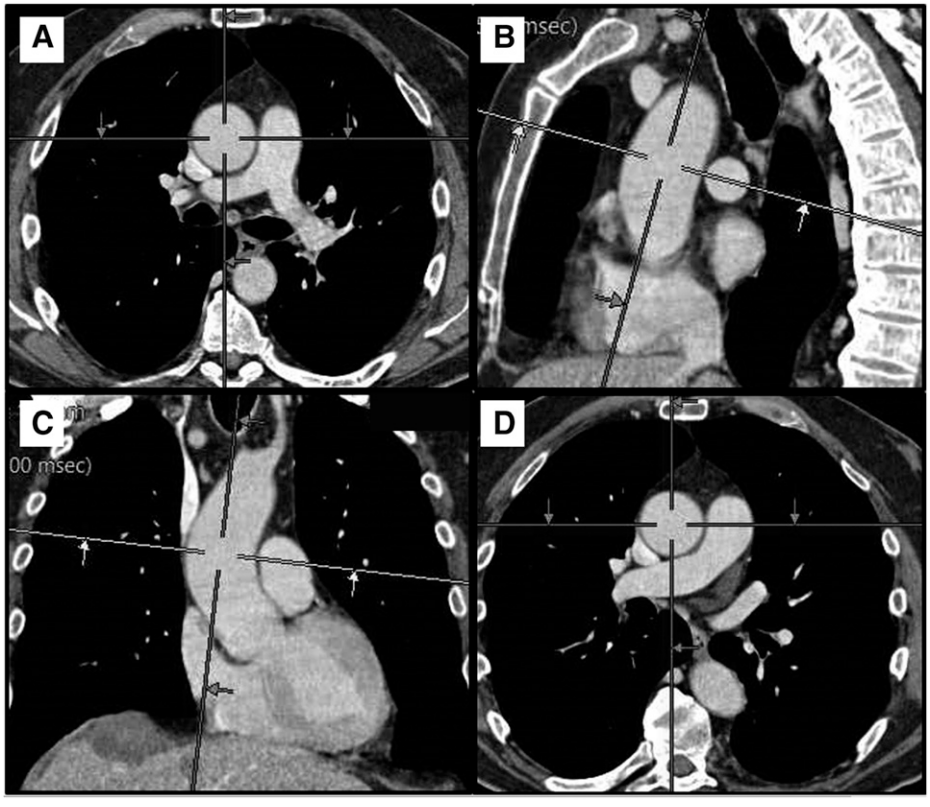
CT scans

Four CT scanners (Somatom Volume Zoom CT system, Siemens Healthineers, Erlangen, Germany; Lightspeed VCT, GE Healthcare, Chicago, IL; Discovery 750, GE Healthcare; Aquilion 16, Toshiba Medical System, Otawara, Tochigi, Japan) were used for all chest CT examinations. Since the study was retrospective, no standard CT protocol was applied.

Three prospective electrocardiography-gated coronary CT and 57 spiral chest CT scans were included in the analyses.

The scanning parameters ranged as follows: tube voltage = 100–140 kVp; tube current = 250–550 mA, pitch = 0.4–1.5;

Figure 2—Standardized method for obtaining the plane perpendicular to the ascending aorta.



(A) The first step consisted in visualizing the axial plane at the bifurcation of the main pulmonary artery. **(B,C)** Correction of the plane along the sagittal and coronal reconstructions, respectively. **(D)** The oblique plane, perpendicular to the ascending aorta, optimized for the measurements of the vessel.

slice reconstructed thickness = 0.63–3 mm; reconstructed slice interval = 0.63–3 mm; reconstruction algorithm (kernel) = smooth (eg, B20f or B30f for Siemens scanner). Thirty CTs were performed after the injection of contrast medium.

In all CTs, it was possible to unequivocally measure the diameters of the AA, DTA, and MPA.

Vascular measurements

AA, DTA, and MPA diameters were calculated according to other previous studies.[29,30] For each patient, an axial slice was identified at the level of pulmonary trunk bifurcation, using a window optimized for mediastinal structures. Since the AA is often not perpendicular to standard planes, multiplanar reformation was used to obtain the real transverse area of the vessel, before proceeding with CT measurements (**Figure 2**). Two dimensions of the outer aortic wall, antero-posterior and latero-lateral, were measured and the average value in millimeters recorded.

At the same level, a similar technique was applied to measure the dimensions of the DTA and the MPA.

Statistical analysis

In all patients with OSA, including the subgroup of participants without comorbidities, a univariate linear analysis with Spearman correlation coefficients was used to assess the possible relations between vascular dimensions (AA, DTA, and MPA) and sleep variables (AHI, ODI, CT90, mean SaO_2, and minimum SaO_2) or demographic parameters (age and BSA). In case of binomial variables (sex, hypertension, type 2 diabetes, COPD) logistic regression analysis was used.

To determine the independent factors, multivariate analysis with a stepwise multiple linear regression model was applied, including AHI, ODI, CT90, mean SaO_2, minimum SaO_2, age, BSA, sex, hypertension, type 2 diabetes, and COPD. This evaluation was not conducted in the subgroup of patients with OSA and without comorbidities due to the reduced number of participants (22).

Among patients with OSA without comorbidities, subjects with different sleep parameters were compared with Mann-Whitney U test for continuous variables and with Fisher exact test for dichotomous variables.

All data analyses were conducted using R statistical software version 1.1.4.63 (R Core Team, Vienna, Austria) and IBM SPSS Statistics for Windows, version 25 (IBM Corp., Armonk, NY).

A $P < .05$ was considered statistically significant.

RESULTS

Characteristics of patients with OSA

Characteristics of the entire population and its 2 subgroups, including demographic and laboratory parameters and comorbidities, are shown in **Table 1**. Data are expressed as median (interquartile range) for continuous variables and as number of patients with the characteristic for dichotomous variables. For the entire population, median age was 65.5 years and only 5 patients were under 50. Most patients were overweight (35%), obese (20%) or extremely obese (23%), and almost two-thirds of patients were males. Thirty-eight patients had one or more cardiovascular or pulmonary comorbidities at history. Most common comorbidities were hypertension, type 2 diabetes, and COPD; only 3 patients had all of these. Other comorbidities were dyslipidemia, valvular heart disease, previous myocardial infarction, or heart failure. Sixty percent of patients had severe OSA. The comparison of the two subgroups of patients, with and without comorbidities,

Table 1—Characteristics of patients with OSA.

	All Patients (n = 60)	Subgroup of Patients with Comorbidities (n = 38)	Subgroup of Patients without Comorbidities (n = 22)	*P* between the Two Subgroups of Patients
Median age (IQ range), years	65.5 (57.2–75.5)	67.5 (62–77)	62.5 (49.5–73)	.087
Male sex, n (%)	41 (68.3%)	26 (68.4%)	15 (68.2%)	.985
Median BSA (IQ range), kg/m^2	2.03 (1.90–2.12)	2.08 (1.87–2.20)	1.99 (1.79–2.12)	.232
Hypertension, n (%)	31 (51.7%)	31 (81.7%)	0 (0)	< .001
Type 2 diabetes, n (%)	13 (21.7%)	13 (34.2%)	0 (0)	.001
COPD, n (%)	8 (13.3%)	8 (21%)	0 (0)	.022
Median AHI (IQ range), events/h	34.3 (19.3–50.5)	34.9 (20.3–50.2)	32.3 (17.7–54.4)	.529
AHI < 30 (nonsevere OSA)	24 (40%)	14 (37%)	10 (45%)	.589
AHI ≥ 30 (severe OSA)	36 (60%)	24 (63%)	12 (55%)	.589
Median ODI (IQ range), n	31.8 (16.9–46.5)	32.1 (20.5–45.4)	26.1 (13.7–48.1)	.5
Median CT90 (IQ range), %	15.65 (3.2–30.7)	17.6 (4.1–30.2)	9.9 (2.5–37.2)	.345
Mean SaO_2 (IQ range), median %	92 (91–94)	92 (91–94)	93 (90.9–94)	.67
Minimum SaO_2 (IQ range), median %	81 (75.5–85)	81 (76.2–84.7)	81 (74–87)	.655

AHI = apnea-hypopnea index, BSA = body surface area, COPD = chronic obstructive pulmonary disease, CT90 = time of oxygen saturation < 90%, IQ = interquartile, ODI = oxygen desaturation index, OSA = obstructive sleep apnea, SaO_2 = nocturnal oxygen saturation.

Table 2—Univariate analysis: Spearman correlations between vascular dimensions and characteristics of patients with OSA.

		Age	Male	BSA	AHI	CT90	ODI	Mean SaO_2	Min SaO_2	Hypertension	Type 2 Diabetes	COPD
AA	Rho coef.	.49	.169	.171	.254	.254	.308	−.253	−.278	.016	.09	.039
	P value	< .001	.02	NS	NS	NS	.017	NS	.038	NS	NS	NS
DTA	Rho coef.	.501	.32	.375	.334	.307	.43	−.299	−.341	.149	.14	.171
	P value	.001	.006	.005	.01	.018	.001	.023	.01	NS	NS	NS
MPA	Rho coef.	.34	−.004	.264	.265	.41	.291	−.337	−.251	.064	.07	.15
	P value	.008	NS	NS	.042	.001	.025	.01	NS	NS	NS	NS

BSA = body surface area, COPD, chronic obstructive pulmonary disease, CT90 = time of oxygen saturation < 90%, DTA = descending thoracic aorta, MPA = main pulmonary artery, ODI = oxygen desaturation index, SaO_2 = nocturnal oxygen saturation.

Table 3—Multivariate analysis: variables predicting vascular dimensions.

	Independent Variables Predicting Vascular Dimension	*P* Value	Unstandardized Coefficient (B)
AA	Logarithm of CT90	.035	1.01
	Age	< .001	0.17
DTA	Age	< .001	0.13
	Male sex	.03	1.74
	BSA	.039	3.65
MPA	Logarithm of CT90	.033	1.21
	Age	.036	0.12

AA = ascending aorta, BSA = body surface area, DTA = descending thoracic aorta, MPA = main pulmonary artery.

evidenced no significant differences for age, sex, BSA, and sleep parameters. The group of patients with in-lab night-polysomnography (n = 17) was not significantly different from the group of patients with home sleep apnea test (n = 43) for age, sex, BSA, AHI, ODI, percentage of time with saturation < 90%, mean SaO_2, and minimum SaO_2.

Univariate analysis and correlations between vascular dimensions and characteristics of patients

In order to evaluate the strength of associations between vascular dimensions and characteristics of patients at univariate analysis, Spearman correlation coefficients were calculated. (**Table 2**).

ODI was correlated with all vascular dimensions. AHI, CT90, and mean SaO_2 were correlated with DTA and MPA sizes. Minimum SaO_2 had a significant association with AA and DTA dimensions. Among these, the 2 strongest correlations were between CT90 and MPA size and between ODI and DTA size (correlation coefficients > .4).

Age was correlated with the dimensions of the 3 vessels, while BSA was correlated only with the dimension of the DTA. Moreover, male sex presented a positive correlation with AA and DTA sizes.

No significant correlations were found between vascular dimensions and the considered comorbidities.

Multivariate analysis

In order to remove the influence of other confounding factors and identify independent variables predicting vascular dimensions, a multivariate analysis was conducted, including AHI, ODI, CT90, mean SaO_2, minimum SaO_2, age, BSA, sex, systemic hypertension, diabetes, and COPD.

The analysis of scatter plots, between vascular variables and sleep parameters, suggested a logarithmic relationship between MPA size vs CT90 values (**Figure 3**).

After the substitution of the logarithm of CT90 for the CT90 in the linear regression model, the results of the

Figure 3—Scatter plot of the main pulmonary artery (MPA) size vs the percentage of time of saturation < 90 (CT90).

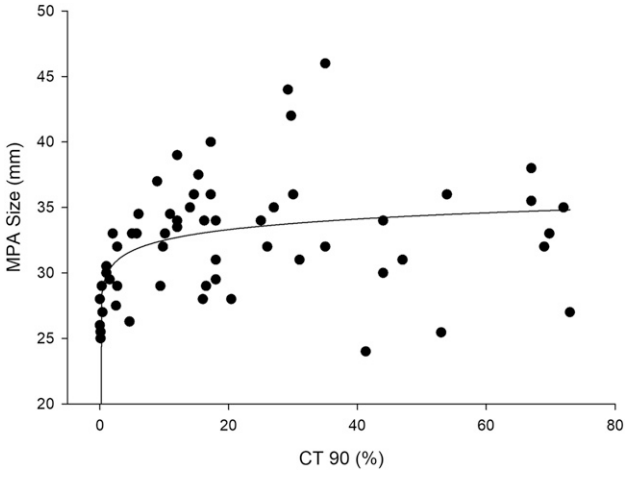
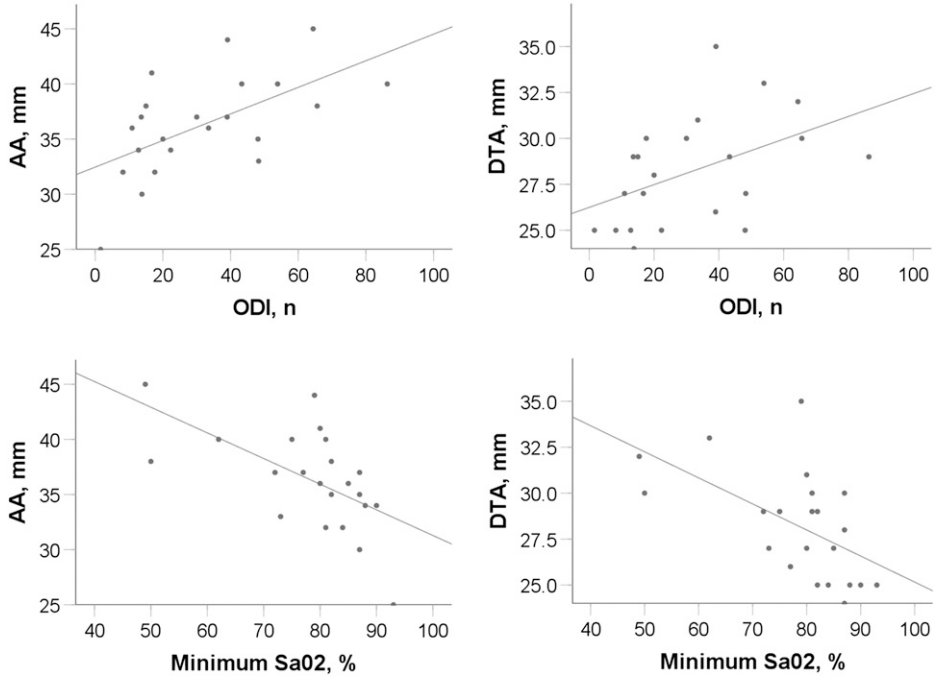


Table 4—Univariate analysis in patients with OSA without comorbidities: correlations between vascular dimensions and characteristics of participants.

		Age	Male	BSA	AHI	ODI	CT90	Mean SaO_2	Min SaO_2
AA	Rho coef.	.473	−.208	.174	.488	.572	.419	−.5	−.643
	P value	.026	NS	NS	.021	.005	NS	.017	.001
DTA	Rho coef.	.494	−.412	.417	.392	.537	.38	−.264	−.637
	P value	.02	NS	NS	NS	.009	NS	NS	.001
MPA	Rho coef.	.456	.000	.485	.164	.297	.418	−.402	−.373
	P value	.033	NS	.022	NS	NS	NS	NS	NS

AA = ascending aorta, DTA = descending thoracic aorta, MPA = main pulmonary artery, SaO_2 = nocturnal oxygen saturation.

Figure 4—Scatterplots of AA and DTA sizes by ODI and minimum SaO_2.



AA = ascending aorta, DTA = descending thoracic aorta, SaO_2 = nocturnal oxygen saturation.

model (Table 3) indicated that the logarithm of CT90 (B = 1.21 *P* = .033), beside age (B = 0.12 *P* = .036), predicted MPA size.

Moreover, AA size was predicted by the logarithms of CT90 (B = 1.01 *P* =.035) and age (B = 0.17 *P* <.001).

DTA size was predicted by age (B = 0.13 *P* <.001), male sex (B = 1.74 *P* =.03), and BSA (B = 3.65 *P* =.039) without a significant association with sleep variables.

Patients with OSA without comorbidities

In the subgroup of 22 patients with OSA without comorbidities, correlations between vascular dimensions and age, sex, BSA, and sleep variables were calculated.

Table 4 summarizes significant correlations between each vascular size (AA, DTA, and MPA) and age, male sex, BSA, AHI, ODI, CT90, mean SaO_2, and minimum SaO_2. The strongest correlations were between ODI and AA and DTA sizes, and between minimum SaO_2 and AA and DTA sizes, as shown in the scatterplots in Figure 4.

Vascular sizes in patients with OSA without comorbidities: comparisons of groups with different ODI or minimum SaO_2

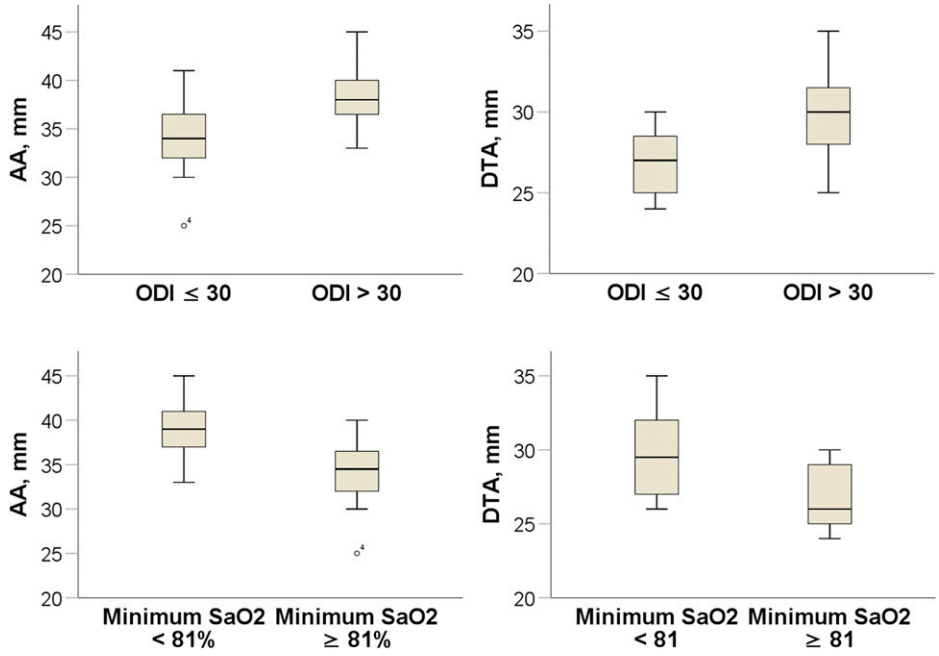
In order to assess, independently from the other parameters, the significant influence of ODI and minimum SaO_2 on vascular diameters in patients with OSA without comorbidities, we compared 2 groups of patients with similar numerosity and different ODI (groups 1 and 2 with ODI ≤ and > 30, respectively) or different minimum SaO_2 (group A and B with minimum SaO_2 < 81 and ≥ 81, respectively) as showed in Table 5. The groups with different ODI or minimum SaO_2 were similar for age, sex, BSA, and MPA. The group with ODI > 30 and the group with minimum SaO_2 < 81 had greater sizes of the AA and DTA (Figure 5) and higher values for the other sleep parameters.

Table 5—Vascular size in patients with different ODI and in patients with different SaO_2.

	Group 1 (ODI ≤ 30) n = 12	Group 2 (ODI > 30) n = 10	*P* Value	Group A (Minimum SaO_2 < 81) n = 10	Group B (Minimum SaO_2 ≥ 81) n = 12	*P* Value
Median age (IQ range), years	55.2 (48.5–75.7)	66.5 (52.2–73)	.468	65.5 (50–73)	59 (48.5–74)	.552
Male sex, n (%)	7 (58.3)	8 (80)	.381	9 (90)	6 (50)	.074
Median BSA (IQ range), kg/m^2	1.9 (1.8–2.1)	2 (1.8–2.2)	.221	1.9 (1.8–2.1)	2 (1.8–2.2)	.884
Median AHI (IQ range), events/h	18.3 (12–23)	54.5 (41.3–57.3)	< .001	44.3 (22.3–55.2)	20.9 (15.2–40.2)	.1
Median ODI (IQ range), n	14.4 (11.4–19.4)	48.2 (39–64)	< .0001	43.7 (17.4–64.7)	17.5 (11.4–32.6)	.017
Median CT90 (IQ range), %	5.8 (0.8–10.7)	25.5 (9.3–67.7)	.018	25.5 (5.2–67.7)	7.3 (0.8–10)	.048
Mean SaO_2 (IQ range), median value, %	93.5 (93–94)	91 (86.8–93)	.006	90.6 (86.8–93)	93.5 (93–94)	.012
Minimum SaO_2 (IQ range), median value, %	86 (81–87.7)	75 (56–80)	.001	74 (59–79)	86 (82–87.7)	< .0001
Median AA size (IQ range), mm	34.5 (32–37)	39 (35.7–41)	.021	39 (36–41.7)	35 (32.5–36.7)	.025
Median DTA size (IQ range), mm	27 (25–29)	29.5 (26.7–32.2)	.043	29.5 (27–32.2)	26 (25–29)	.025
Median MPA size (IQ range), mm	33 (28.2–34)	32.5 (28.7–35.6)	.674	32.4 (29.5–34.7)	33 (27.5–34)	.582

AA = ascending aorta, AHI = apnea-hypopnea index, BSA = body surface area, CT90 = time of oxygen saturation < 90%, DTA = descending thoracic aorta, IQ, interquartile, MPA = main pulmonary artery, ODI = oxygen desaturation index, SaO_2 = nocturnal oxygen saturation.

Figure 5—Boxplots showing AA and DTA sizes in patients with obstructive sleep apnea.



Top: patients without comorbidities and with ODI ≤ 30 and > 30. Bottom: patients with minimum SaO_2 < 81 and ≥ 81. SaO_2 = nocturnal oxygen saturation, AA = ascending aorta, DTA = descending thoracic aorta, ODI = oxygen desaturation index, SaO_2 = nocturnal oxygen saturation.

DISCUSSION

Our analysis considered a group of patients with untreated OSA, including participants with frequently associated cardiovascular comorbidities.

Multivariate regression analysis suggested that the logarithm of CT90 predicted AA and MPA sizes. The influence of sleep variables on dimensions of great thoracic vessels was confirmed in the subgroup of patients with OSA and without comorbidities. In this group, patients with ODI > 30 or minimum SaO_2 < 81 had greater sizes of the AA and DTA.

These results are important because aortic dilation can evolve in aneurysm, with a greater risk of rupture or dissection.[31] A meta-analysis and a prospective study recently evidenced, respectively, a higher risk of aortic dissection in patients with OSA and a higher prevalence of OSA in patients with thoracic aortic aneurysms, compared to the general population.[32,33] However, a recent nationwide retrospective analysis by Shih

et al.[34] did not find an association between OSA and aortic aneurysm, in the Taiwan population.

In the whole cohort and in participants without comorbidities, sleep variables associated with vascular dimensions were directly dependent on oxygen desaturation, suggesting that hypoxia could play a key role in vascular remodeling.

MPA size was predicted by the logarithm of CT90 in all patients with OSA, but no associations with sleep variables were noted in the subgroup of patients with OSA and without comorbidities. A possible explanation is that MPA size could be affected by cardiovascular and pulmonary comorbidities associated with OSA, rather than by OSA itself, through the mechanisms of intrathoracic negative pressure changes and systemic inflammation. Since comorbidities are frequently present in patients with a more severe stage of OSA, we may also expect greater MPA size in these patients.

The analysis of patients with a dilatation of the AA led to interesting considerations. AA size > 40 mm was present in 14 patients with OSA with associated comorbidities out of 38 (36%) and in 6 patients with OSA without comorbidities out of 22 (27%). The 14 participants with comorbidities had less severe values of sleep parameters than the 6 patients without comorbidities. In the patients with OSA with comorbidities, median AHI, ODI, CT90, mean SaO_2, and minimum SaO_2 were 33.3, 31.7, 17.6, 91.6, and 81, respectively; in the patients with OSA without comorbidities, the same sleep parameters were 55.8, 48.6, 22.9, 90.6, and 77, respectively. This difference may indicate an earlier AA remodeling in patients with comorbidities.

The association we found between sleep parameters and AA size is consistent with the results of previous studies[15–19] and in contrast with other authors.[20–23] Our study aimed to make a contribution on this topic, trying to overcome some of the limitations identifiable in previous studies. In particular, one of these studies[21] did not take into account the fact that some patients were being treated for OSA, leading to an underestimation of the severity of the disease in those subjects. In 3 other studies[15,16,22] that did not include patients with OSA with low AHI (AHI < 10 events/h[15,18] or < 15 events/h[16,21]), current diagnostic criteria for OSA were not applied. Two studies[15,17] considered only 1 sleep parameter, the AHI, and did not assess possible associations with other sleep variables. In some other research works,[16,17,21] a multivariate analysis of important factors potentially influencing AA diameter (such as age, BSA or BMI, and sex) was not conducted. In 1 study, the population was a group of patients with acute myocardial infarction,[22] a comorbidity that could affect the measurements of the AA root. In previous research works,[15–19,21–23] different anatomic landmarks were considered and, since echocardiography was often used to measure vessels, there was a lack of information about the dimensions of the DTA and the MPA.

Our study was innovative for 2 additional aspects. First, we used a CT approach to assess not only the AA but also the DTA and the MPA. Second, we selected and also separately analyzed patients with OSA without comorbidities. Since OSA is a complex disease and associated with several comorbidities, this type of analysis could be fundamental to assessing the different effects that this condition, alone or with comorbidities, might have on great thoracic vessels.

Limitations

Significant limitations are present in our study.

First, the study was retrospective. At the time of clinical evaluation, the smoking status of patients and occupational pulmonary exposure were not recorded, and we could not include them in the analysis. Positive smoking status is a parameter that potentially influences the dimensions of the great thoracic vessels. The issue is still controversial as a few papers have consistently shown that smoking increases the diameter of the descending tract of aorta only,[29,35,36] while a recent study suggested that both ascending and descending aortic dimensions across age in current or former smokers are instead comparable with those of nonsmoking population.[37]

Second, the study did not include a control group of patients without obstructive sleep apnea. These considerations suggest that these results may need to be confirmed in a future prospective study with a wider cohort of patients and a control group.

Moreover, the actual knowledge of OSA impact on thoracic great vessels does not support CT as a screening procedure, due to concerns related to radiation exposure. In fact, unlike ultrasound, CT has the disadvantage of exposing patients to ionizing radiations. Since a linear no-threshold model is commonly accepted for the risk of radiation-related cancer, all CT exams must have a clinical justification.

CONCLUSIONS

In conclusion, our study found that CT90 may influence AA and MPA sizes in patients with OSA, while in the subgroup of patients without comorbidities, ODI and minimum SaO_2 were moderately correlated with AA and DTA sizes. It emerged that patients without comorbidities and with ODI > 30 or minimum SaO_2 < 81 had greater AA and DTA sizes than patients with, respectively, ODI ≤ 30 or SaO_2 ≥ 81, while age, sex, and BSA did not present significant differences in the two groups.

ABBREVIATIONS

AA, ascending aorta
AHI, apnea-hypopnea index
BSA, body surface area
COPD, chronic obstructive pulmonary disease
CT, computed tomography
CT90, time of oxygen saturation < 90%
DTA, descending thoracic aorta
MPA, main pulmonary artery
ODI, oxygen desaturation index
OSA, obstructive sleep apnea
SaO_2, nocturnal oxygen saturation

REFERENCES

1. Floras JS. Sleep apnea and cardiovascular disease: an enigmatic risk factor. *Circ Res*. 2018;122(12):1741–1764.
2. Gaisl T, Bratton DJ, Kohler M. The impact of obstructive sleep apnea on the aorta. *Eur Respir J*. 2015;46(2):532–544.

3. Peters J, Kindred MK, Robotham JL. Transient analysis of cardiopulmonary interactions. II. Systolic events. *J Appl Physiol*. 1988;64(4):1518–1526.
4. Peters J, Kindred MK, Robotham JL. Transient analysis of cardiopulmonary interactions. I. Diastolic events. *J Appl Physiol*. 1988;64(4):1506–1517.
5. Suzuki M, Ogawa H, Okabe S, et al. Digital recording and analysis of esophageal pressure for patients with obstructive sleep apnea-hypopnea syndrome. *Sleep Breath*. 2005;9(2):64–72.
6. Stöwhas AC, Namdar M, Biaggi P, et al. The effect of simulated obstructive apnea and hypopnea on aortic diameter and BP. *Chest*. 2011;140(3):675–680.
7. Cutler MJ, Swift NM, Keller DM, Wasmund WL, Smith ML. Hypoxia-mediated prolonged elevation of sympathetic nerve activity after periods of intermittent hypoxic apnea. *J Appl Physiol*. 2004;96(2):754–761.
8. Bisogni V, Pengo MF, Maiolino G, Rossi GP. The sympathetic nervous system and catecholamines metabolism in obstructive sleep apnea. *J Thorac Dis*. 2016; 8(2):243–254.
9. Maleszewski JJ. Inflammatory ascending aortic disease: perspectives from pathology. *J Thorac Cardiovasc Surg*. 2015149, 2, Suppl:S176–S183.
10. Bruno RM, Rossi L, Fabbrini M, et al. Renal vasodilating capacity and endothelial function are impaired in patients with obstructive sleep apnea syndrome and no traditional cardiovascular risk factors. *J Hypertens*. 2013;31(7): 1456–1464, discussion 1464.
11. Mancuso M, Bonanni E, LoGerfo A, et al. Oxidative stress biomarkers in patients with untreated obstructive sleep apnea syndrome. *Sleep Med*. 2012;13(6): 632–636.
12. Nadeem R, Molnar J, Madbouly EM, et al. Serum inflammatory markers in obstructive sleep apnea: a meta-analysis. *J Clin Sleep Med*. 2013;9(10):1003–1012.
13. Gileles-Hillel A, Almendros I, Khalyfa A, Zhang SX, Wang Y, Gozal D. Early intermittent hypoxia induces proatherogenic changes in aortic wall macrophages in a murine model of obstructive sleep apnea. *Am J Respir Crit Care Med*. 2014; 190(8):958–961.
14. Gileles-Hillel A, Almendros I, Khalyfa A, et al. Prolonged exposures to intermittent hypoxia promote visceral white adipose tissue inflammation in a murine model of severe sleep apnea: effect of normoxic recovery. *Sleep*. 2017;40(3) .
15. Serizawa N, Yumino D, Takagi A, et al. Obstructive sleep apnea is associated with greater thoracic aortic size. *J Am Coll Cardiol*. 2008;52(10):885–886.
16. Cicek D, Lakadamyali H, Yağbasan BD, Sapmaz I, Müderrisoğlu H. Obstructive sleep apnea and its association with left ventricular function and aortic root parameters in newly diagnosed, untreated patients: a prospective study. *J Int Med Res*. 2011;39(6):2228–2238.
17. Chen YL, Su MC, Liu WH, Wang CC, Lin MC, Chen MC. Influence and predicting variables of obstructive sleep apnea on cardiac function and remodeling in patients without congestive heart failure. *J Clin Sleep Med*. 2014;10(1):57–64.
18. Baguet J-P, Minville C, Tamisier R, et al. Increased aortic root size is associated with nocturnal hypoxia and diastolic blood pressure in obstructive sleep apnea. *Sleep*. 2011;34(11):1605–1607.
19. Achour EC, Roche F, Romeyer-Bouchard C, et al. Aortic root size and sleep apnea in elderly: a cohort study. *Int J Cardiol*. 2011;151(1):101–102.
20. Cicco S, Castellana G, Marra L, et al. Analysis of aortic remodeling and stiffness in patients with obstructive sleep apnea syndrome: preliminary results. *Adv Exp Med Biol*. 2018;1072:251–255.
21. Meuleman C, Boccara F, Nguyen X-L, et al. Is the aortic root dilated in obstructive sleep apnea syndrome? *Arch Cardiovasc Dis*. 2008;101(6):391–397.
22. Lee LC, Torres MC, Khoo SM, et al. The relative impact of obstructive sleep apnea and hypertension on the structural and functional changes of the thoracic aorta. *Sleep*. 2010;33(9):1173–1176.
23. Tanriverdi H, Evrengul H, Kara CO, et al. Aortic stiffness, flow-mediated dilatation and carotid intima-media thickness in obstructive sleep apnea: non-invasive indicators of atherosclerosis. *Respiration*. 2006;73(6):741–750.
24. Atwood CW Jr, McCrory D, Garcia JG, Abman SH, Ahearn GS; American College of Chest Physicians. Pulmonary artery hypertension and sleep-disordered breathing: ACCP evidence-based clinical practice guidelines. *Chest*. 2004;126(1 Suppl):72S–77S.
25. Minai OA, Ricaurte B, Kaw R, et al. Frequency and impact of pulmonary hypertension in patients with obstructive sleep apnea syndrome. *Am J Cardiol*. 2009;104(9):1300–1306.
26. Sateia MJ. International classification of sleep disorders-third edition: highlights and modifications. *Chest*. 2014;146(5):1387–1394.
27. Kapur VK, Auckley DH, Chowdhuri S, et al. Clinical practice guideline for diagnostic testing for adult obstructive sleep apnea: an American Academy of Sleep Medicine clinical practice guideline. *J Clin Sleep Med*. 2017;13(3):479–504.
28. American Academy of Sleep Medicine. The AASM Manual for the Scoring of Sleep and Associated Events. Summary of Updates in Version 2.5. https://aasm.org/wp-content/uploads/2018/04/Summary-of-Updates-in-v2.5-1.pdf. Published April 2, 2018. Accessed September 3, 2020.
29. Wolak A, Gransar H, Thomson LE, et al. Aortic size assessment by noncontrast cardiac computed tomography: normal limits by age, gender, and body surface area. *JACC Cardiovasc Imaging*. 2008;1(2):200–209.
30. Raymond TE, Khabbaza JE, Yadav R, Tonelli AR. Significance of main pulmonary artery dilation on imaging studies. *Ann Am Thorac Soc*. 2014;11(10):1623–1632.
31. Elefteriades JA. Thoracic aortic aneurysm: reading the enemy's playbook. *Curr Probl Cardiol*. 2008;33(5):203–277.
32. Gaisl T, Baumgartner P, Rejmer P, et al. Prevalence of obstructive sleep apnea in patients with thoracic aortic aneurysm: a prospective, parallel cohort study. *Respiration*. 2020;99(1):19–27.
33. Zhou X, Liu F, Zhang W, et al. Obstructive sleep apnea and risk of aortic dissection: a meta-analysis of observational studies. *Vascular*. 2018;26(5):515–523.
34. Shih CC, Wang JC, Tsai SH, et al. Obstructive sleep apnea and aortic aneu rysm: a nationwide population-based retrospective study. *J Vasc Res*. 2018;55(4): 235–243.
35. Mensel B, Heßelbarth L, Wenzel M, et al. Thoracic and abdominal aortic diameters in a general population: MRI-based reference values and association with age and cardiovascular risk factors. *Eur Radiol*. 2016;26(4):969–978.
36. Truong QA, Massaro JM, Rogers IS, et al. Reference values for normal pulmonary artery dimensions by noncontrast cardiac computed tomography: the Framingham Heart Study. *Circ Cardiovasc Imaging*. 2012;5(1):147–154.
37. Bons LR, Sedghi Gamechi Z, Thijssen CGE, et al. Growth of the thoracic aorta in the smoking population: The Danish Lung Cancer Screening Trial. *Int J Cardiol*. 2020;299:276–281.

ACKNOWLEDGMENTS

The authors acknowledge the continuous support of Prof. Davide Caramella (University of Pisa, Italy) in all phases of our work, as well as the help given by Prof. Paolo Frumento (Karolinska Institutet, Stockholm, Sweden) for the development of the statistical model.

SUBMISSION & CORRESPONDENCE INFORMATION

Submitted for publication March 31, 2020
Submitted in final revised form August 17, 2020
Accepted for publication August 17, 2020
Address correspondence to: Roberto Castellana, MD, Diagnostic and Interventional Radiology, University of Pisa, Via Paradisa 2, 56124 Pisa, Italy; Tel: +39 3291893534; Email: r.castellana1@studenti.unipi.it

DISCLOSURE STATEMENT

All authors have seen and approved the manuscript. Work for this study was performed at Pisa University Hospital. The authors report no conflicts of interest.