Journal of the American College of Cardiology
© 2008 by the American College of Cardiology Foundation
Published by Elsevier Inc.

Vol. 52, No. 10, 2008
ISSN 0735-1097/08/$34.00

CORRESPONDENCE

Research Correspondence

Obstructive Sleep Apnea Is Associated With Greater Thoracic Aortic Size

To the Editor: Obstructive sleep apnea (OSA), characterized by partial or complete occlusion of the pharynx during sleep, results in persistent inspiratory effort and interruption of airflow. During each episode of apnea, OSA patients develop increased transmural pressure in the aortic wall. Accordingly, to test the hypothesis that the presence of OSA would be associated with greater thoracic aortic size, we prospectively assessed 150 consecutive patients, newly referred to the sleep clinic in our institution, in a cross-sectional study to confirm OSA. The patients underwent sleep study and chest computed tomography (CT)-derived thoracic aortic diameter. In this particular period, a chest CT was performed within 3 months of the sleep study upon informed consent to our protocol. Exclusion criteria included: 1) prior history of aortic dissection, aortic valvular disease, and clinical characteristics of Marfan's syndrome; 2) central sleep apnea; 3) treatment for sleep apnea; and 4) dialysis. The outer diameter of the ascending aorta was measured by caliper within the CT image. Overnight sleep study was performed using cardiopulmonary monitoring (Morpheus, Teijin Inc., Tokyo, Japan). The apnea-hypopnea index (AHI) was quantified as the frequency of apneas and hypopneas per hour of bed time. OSA was defined as AHI ≥10/h. The data are presented as mean ± SD or frequencies. To determine the independent factors, the multiple linear regression model with backward elimination technique was used, including older age, male gender, blood pressure, hypertension, dyslipidemia, diabetes mellitus, ischemic heart disease, smoking, and AHI. Comparisons between the 2 groups were performed by Student *t* test for the unadjusted aortic diameter and by analysis of covariance for the adjusted aortic diameter.

The patients' mean age was 60 ± 11 years; 125 (83%) were men, with mean body mass index of 24.7 ± 3.1 kg/m^2. Fifty-nine percent of patients had hypertension. At assessment, 91% of patients had already taken prescribed antihypertensive medications. One hundred ten patients (73%) had OSA. On univariate analysis, older age, male gender, body mass index, systolic blood pressure, pulse pressure, hypertension, dyslipidemia, ischemic heart disease, and AHI were positively correlated with thoracic aortic size. On multivariate analysis, older age (per 10-year increase, coefficient 1.82, 95% confidence interval [CI]: 1.13 to 2.34, $p < 0.001$), male gender (coefficient 3.25, 95% CI: 1.63 to 4.87, $p < 0.001$), and AHI (per 10-event/h increase, coefficient 0.62, 95% CI: 0.25 to 0.98, $p < 0.001$) remained as factors associated with greater thoracic aortic diameter. Contrarily, there was no significant independent relationship between blood pressure/hypertension and thoracic aortic size. Additionally, patients with OSA had a significantly greater thoracic aortic size than those without OSA ($p < 0.001$) (Fig. 1), even if adjusted for older age and male gender ($p < 0.001$).

Increased thoracic aortic size is known to be related to aging, male, genetic mutation including Marfan's syndrome, hypertension, and atherosclerosis. There are few published papers comparable to this study. Cistulli et al. (1) reported 2 cases of Marfan's syndrome in which treatment of OSA by continuous positive airway pressure associated with a marked attenuation in the aortic dilatation. Sampol et al. (2) reported 19 patients with thoracic aortic dissection who had a high prevalence of severe OSA. The effect of hypertension on greater thoracic aortic size is accepted. For example, Dapunt et al. (3) reported that a history of hypertension was correlated with greater aortic size. However, Masuda et al. (4) and we did not find a significant independent correlation of blood pressure/hypertension on multivariate analysis; it may be difficult to exclude such a correlation as an important contributor to greater thoracic aortic size in already medicated patients. In addition, OSA can contribute to the development of hypertension. Our data suggested that OSA may contribute to increased thoracic aortic size not only by causing hypertension but also through mechanical stress on the aortic wall from repeated episodes of apneas and hypopnea. Inspiratory effort against occluded upper airway during an OSA episode results in negative intrathoracic pressures as low as −80 cm H_2O, which can affect intrathoracic hemodynamics. Peters et al. (5) reported that, in rats, decreased intrathoracic pressure during diastole can distend the intrathoracic aorta. Thus, repeated episodes of sudden increments and changes in the transmural pressure of the aortic wall could contribute to

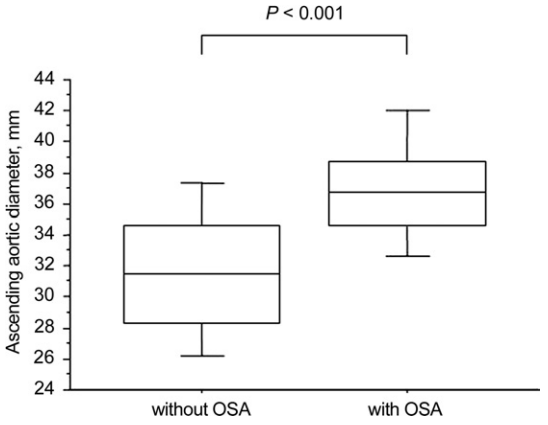

Figure 1 **Obstructive Sleep Apnea and Ascending Aortic Diameter**

Box plot showing ascending aortic diameter between patients without obstructive sleep apnea (OSA) (n = 40) and with OSA (n = 110). **Middle horizontal line inside box** indicates the means. The **bottom and top of the box** are the 25th and 75th percentiles, respectively. Thoracic aortic size was significantly greater in patients with OSA than in those without OSA (36.8 ± 3.6 mm vs. 31.5 ± 4.5 mm, $p < 0.001$), even if adjusted for older age and male gender ($p < 0.001$).

increased thoracic aortic size. Our observations had a main limitation: because the present study was based on cross-sectional data, it is difficult to prove that OSA accelerates aortic expansion.

The present study indicates that OSA could contribute to greater thoracic aortic size.

Acknowledgments

The authors thank Katsunori Shimada (STATZ Institute Inc., Tokyo, Japan) for expert statistical assistance and are indebted to Koichi Takeuchi and Reiko Ohnishi for their excellent technical assistance.

Naoki Serizawa, MD
***Dai Yumino, MD**
Atsushi Takagi, MD
Keiko Gomita, MD
Katsuya Kajimoto, MD
Yukio Tsurumi, MD
Nobuhisa Hagiwara, MD

*Department of Cardiology
Tokyo Women's Medical University
8-1 Kawada-cho, Shinjuku-ku
Tokyo 162-8666
Japan
E-mail: yumino@mvj.biglobe.ne.jp

doi:10.1016/j.jacc.2008.05.039

REFERENCES

1. Cistulli PA, Wilcox I, Jeremy R, Sullivan CE. Aortic root dilatation in Marfan's syndrome: a contribution from obstructive sleep apnea? Chest 1997;111:1763–6.
2. Sampol G, Romero O, Salas A, et al. Obstructive sleep apnea and thoracic aorta dissection. Am J Respir Crit Care Med 2003;168:1528–31.
3. Dapunt OE, Galla JD, Sadeghi AM, et al. The natural history of thoracic aortic aneurysms. J Thorac Cardiovasc Surg 1994;107:1323–32, discussion 1332–3.
4. Masuda Y, Takanashi K, Takasu J, Morooka N, Inagaki Y. Expansion rate of thoracic aortic aneurysms and influencing factors. Chest 1992; 102:461–6.
5. Peters J, Kindred MK, Robotham JL. Transient analysis of cardiopulmonary interactions. I. Diastolic events. J Appl Physiol 1988;64:1506–17.

Letters to the Editor

Limitations of Angiographic Predictors of Bypass Graft Patency

I compliment the work of Glineur et al. (1) on advancing our appreciation of the physiologic predictors of 6-month patency rates of bypass grafts to the right coronary artery. The patency of the gastroepiploic artery (GEA) had a significant association with minimal luminal diameter (MLD) and percent diameter stenosis, angiographic features that did not affect saphenous vein graft patency rates as much. A larger MLD (>1.4 mm) and the percent diameter stenosis (<55% narrowing) predicted GEA graft closure. The accompanying editorial by Sabik and Blackstone (2) expertly reviewed the evidence for competitive flow and coronary artery bypass graft patency, explaining some of the factors in play for the outcomes reported by Glineur et al. (1).

Although competitive flow between native and grafted coronary vessels has been known to surgeons for many years as a cause of graft failure (3–5), the prediction of graft patency on the basis of the physiology of competitive flow should not be judged by angiography alone. The numerous studies on intracoronary pressure and intravascular ultrasound imaging reinforce the failure of the angiogram to provide important physiologic and true anatomic information, especially for intermediately severe stenoses (6,7). Using angiography as a surrogate for physiologic activity is often erroneous and, at this time, is an imprecise technique when addressing physiologic mechanisms as described by Sabik et al. (5) and others (3,4). The competing flow potential of the native artery with vein graft flow can be directly measured by coronary pressure or Doppler flow in patients in the cardiac catheterization laboratory (6,8).

The measurement of hyperemic translesional pressure ratio, called fractional flow reserve (FFR) (8,9), has been applied to study the fate of coronary bypass grafts with striking results. Confirming the relevance of the physiologic stenosis severity and graft patency, Botman et al. (10) report the 1-year follow-up of 164 patients undergoing coronary bypass grafts. All vessels grafted had FFR measured beforehand with the pressure sensor angioplasty guidewire in the catheterization laboratory. At 1 year, 9% of grafts on functionally significant lesions were occluded, whereas 21% of grafts on functionally nonsignificant lesions were occluded. A significant graft occlusion rate was observed for grafted vessels with near normal physiology (FFR >0.80, normal = 1.0). The angiographic percent diameter narrowings displayed a similar but less precise correlation with graft failure. The findings from Botman et al. (10) again emphasize what is generally appreciated but unmeasured: that is, the physiologic impact of intermediately severe stenosis remains unknown by angiography.

Whereas the angiographic descriptor of MLD provided by Glineur et al. (1) is an advance over measurements of stenosis diameter (even if using a quantitative angiographic imaging system), the precise pressure across stenosis can be obtained often without difficulty by most interventional cardiologists. Certainly, severe narrowings and total occlusions do not need such direct measurements, but the physiologic assessment of intermediate lesions can assist selection of the appropriate bypass graft should the surgeon have an interest in this approach (11).

Sabik and Blackstone (2) note that using only maximal coronary artery stenosis would not adjust for coronary artery size, whereas MLD does this to a larger extent. However, neither MLD of the reference lumen diameter nor percent lumen diameter narrowing truly reflects competitive flow physiology. Although I recognize this might not be possible in many clinical settings, I believe