Silent Bedpartners
Obstructive Sleep Apnea and Hypertension, 6 Years Later

In 1996, I wrote an editorial discussing the relationship between obstructive sleep apnea (OSA) and hypertension. In that issue of CHEST, Coy et al² presented data supporting the link between these two common disorders. They examined patients with OSA to determine if the severity of OSA as defined by the apnea-hypopnea index (AHI) was correlated with the presence of hypertension. Indeed, AHI was correlated with an elevated diastolic BP, independent of body mass index and age.

New information has subsequently become available to further define this relationship. Two large epidemiologic studies showed increasing odds ratios for the presence of hypertension related to the severity of OSA as defined by the AHI.³,⁴ In both articles, this relationship persisted even after adjusting for a variety of confounding variables often noted in the patient populations with these disorders (age, gender, body mass index, tobacco use, etc). These again showed OSA and hypertension are clearly linked, without conferring causality.

One approach to establishing causation would be to demonstrate that treatment of OSA mitigates hypertension. Although several studies have used this approach,⁵⁻⁹ the study in this issue of CHEST (see page 1125) is the only one to use a hypertensive, nonapneic control group and treat them with nasal continuous positive airway pressure (CPAP). The experimental design, therefore, examined the possibility that CPAP itself may alter BP unassociated with any effects it may have on eliminating OSA. Another unique aspect of this study was that the recruited study population was hypertensive patients rather than patients with OSA, and was reportedly “asymptomatic” with regards to the presence of hypersomnia and/or sleep fragmentation.

The study participants wore nasal CPAP for 3 weeks, during which time the authors noted a significant change in nocturnal BP in the OSA group with a similar trend of decreasing daytime BP. The control group had no significant change in BP with CPAP, suggesting the CPAP itself does not alter BP independent of its effect on OSA.

There are some notable limitations of this study. Nasal CPAP is an onerous therapy, particularly if the person wearing it receives no benefit from its use. As would be expected, the control group was not as compliant with CPAP as the OSA group, raising the possibility that hypertension was not improved in the control population because they did not wear their CPAP as frequently. The difference in CPAP adherence between the groups could also suggest that symptoms were less “occult” than suggested, as they used their CPAP much more than the control subjects (5.7 ± 1.7 hours per night vs 3.5 ± 2.2 hours per night). Unfortunately, no measurements of subjective or objective sleepiness were reported.

As we inch inexorably closer to confirming that OSA can cause diurnal hypertension, additional questions arise. Does OSA-induced hypertension have the same cardiovascular consequences as hypertension from other causes? Should hypertensive patients with milder forms of OSA be treated more aggressively with regard to their OSA than nonhypertensive OSA patients? What is the mechanism explaining why some OSA patients acquire hypertension and others do not? The outcome data, as are being collected in the Sleep Heart Health Study and Wisconsin Cohort Study, should help answer some of these questions.

It appears that OSA is a contributing risk factor for cardiovascular disease. Physicians treating patients with hypertension should now consider OSA in their differential diagnosis of all patients with hypertension.

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REFERENCES
Lung Transplantation and Bronchiolitis Obliterans Syndrome

Are Two Lungs Better Than One?

The current survival rates for lung transplant recipients are 72%, 56%, and 43%, respectively, at 1, 3, and 5 years, as reported by the registry of the International Society of Heart and Lung Transplantation (ISHLT). These data can be further subanalyzed based on single-lung transplant (SLT) vs bilateral lung transplant (BLT) procedures. SLT survival rates were 71%, 54%, and 40% at 1, 3, and 5 years, respectively. BLT survival rates were 72%, 58%, and 48% at 1, 3, and 5 years, respectively.

The leading cause of mortality after the first year following transplantation is bronchiolitis obliterans, with an incidence of 30 to 50%. Bronchiolitis obliterans has become the sine qua non for chronic lung rejection in the lung transplant population. Bronchiolitis obliterans presents clinically with an obstructive deterioration in pulmonary function and little change in chest radiograph appearance, and it develops >3 to 6 months following transplantation, usually at a mean of 16 to 20 months. Pathologically, there is obliteration of the terminal bronchioles (ie, constrictive bronchiolitis). Because it is difficult to make a reliable histologic diagnosis of bronchiolitis, the ISHLT has defined a bronchiolitis obliterans syndrome (BOS) staging system based on a deterioration of pulmonary function (FEV₁ reported as a percentage of posttransplant baseline values) with the performance of bronchoscopy to exclude alternate diagnoses such as acute rejection, infection, or anastomotic complications. The staging system is further subdivided by the presence or absence of the histologic confirmation of bronchiolitis. Since the sensitivity of transbronchial biopsy for the pathologic diagnosis of BOS can be as low as 15%, in the majority of cases the diagnosis of BOS is made based on pulmonary function changes alone.

The etiology of BOS remains unknown, although numerous risk factors have been postulated. Probable risk factors for BOS include acute rejection, lymphocytic bronchitis, and cytomegalovirus (CMV) pneumonitis. Other potential or hypothetical risk factors include CMV infection, organizing pneumonia, non-CMV infection, older donor age, prolonged ischemic time, human leukocyte antigen mismatching, and donor antigen-specific reactivity.

As illustrated earlier in the ISHLT survival data, there is increased survival in all patients undergoing BLT vs those undergoing SLT procedures by 3 years following transplantation. The reasons for this are unclear but have been speculated to be due to greater pulmonary function reserve in BLT recipients. The article in this issue of CHEST by Hadjiliadis et al (see page 1168) proposes a hereto unreported risk factor for BOS and postulates a hypothesis to explain the survival differences noted.

This is a retrospective study from a single large lung transplant center comparing a group of patients undergoing BLT to those undergoing SLT with respect to the development of BOS. When numerous risk factors were subjected to several types of multivariate analyses, the authors found the following risk factors to correlate with the development of BOS: acute rejection scores; the number of human leukocyte antigen mismatches; CMV mismatch; and, the focus of the article, the type of lung transplant procedure performed. In fact, procedure type was found to be an independent risk factor for BOS in all of the analyses conducted. The authors found that, at least in a relatively short follow-up period (median follow-up, 2.4 years; range, 1.5 to 4 years), the BLT group had a significantly lower incidence of developing BOS (31.7%) than did the SLT group (49.3%).

The other BOS risk factors identified in this analysis have been reported previously in multiple studies. This is the first report of a difference in the incidence of BOS between patients who have undergone SLT procedures and those who have undergone BLT procedures. Since the cellular and immu-