Obstructive Sleep Apnea and Cardiovascular Disease

Sleep-disordered breathing is a common condition affecting up to 9% of middle-aged women and 24% of middle-aged men. It often interferes with sleep and is a major cause of daytime somnolence, affecting quality of life and having a major impact on the workplace. Obstructive sleep apnea (OSA) is one of the more serious clinical manifestations of sleep-disordered breathing. OSA is typically caused by intermittent airway obstruction (due to weakness of the pharyngeal musculature with resultant collapse of the airway), interfering with normal inspiration. The increased inspiratory effort leads to labored breathing and may profoundly disturb sleep due to frequent and abrupt awakenings as the individual struggles to breathe. Total collapse of the airway with complete obstruction for periods of 10 s or more is considered obstructive apnea, while partial airway obstruction (30 to 99%) associated with arterial desaturation is termed obstructive hypopnea.

OSA severity is typically assessed by means of an apnea-hypopnea index, determined by the ratio of the number of apneic and hypopneic episodes per hour of sleep. It is generally thought that up to 5 episodes per hour can occur in normal individuals, while patients with severe OSA can have in excess of 30 episodes per hour, producing significant arterial desaturation and profound disruption of sleep. It is estimated that 2% of middle-aged women and 4% of middle-aged men have five or more apnea/hypopnea episodes per hour and meet criteria for OSA. There are several risk factors for OSA, with male gender and especially obesity most prominent among them.

OSA has been reported to be associated with an increased mortality. Some of the excess mortality is clearly due to trauma related to daytime sleepiness (automobile accidents, accidents in the workplace, etc), but the increased incidence of cardiovascular disorders reported in patients with OSA is also likely to play a role.

There appear to be multiple mechanisms that may explain the relationship between OSA and cardiovascular disease. It is hypothesized that the frequent apneic/hypopneic episodes and the resulting arterial desaturation and hypercapnia cause activation of the sympathetic nervous system, resulting in frequent surges in systolic BP that eventually lead to hypertension. A similar mechanism is postulated for the described relationship between OSA and tachyarrhythmias, especially atrial fibrillation. In contrast, bradyarrhythmias are probably related to an increase in vagal tone due to stimulation of upper airway receptors. Other abnormalities described in OSA that may be involved in the pathogenesis of cardiovascular disease include disorders in coagulation factors, endothelial damage (in part related to abnormal leukocyte adhesion and aggregation), platelet activation, and an increase in inflammatory mediators. Many of these factors, along with the high prevalence of systemic hypertension, appear responsible for the increased incidence of stroke observed in patients with OSA.

There is a high incidence of OSA in patients with idiopathic dilated cardiomyopathy, especially when there is superimposed congestive heart failure. There are several possible mechanisms by which OSA may be involved in the causation of congestive heart failure. Heart failure (and the Cheyne-Stokes respiration pattern that is frequently encountered in heart failure patients) may reduce the drive to the pharyngeal musculature, facilitating pharyngeal collapse. Similarly, edema of the pharyngeal wall associated with central venous pressure elevation can produce luminal narrowing and predispose to collapse of the airway. Systemic hypertension undoubtedly also contributes to the development of congestive heart failure. The neurohumoral activation and increase in inflammatory mediators associated with abrupt increases in sympathetic tone, especially combined with arterial desaturation and the metabolic disturbances of OSA, are likely to result in depressed left ventricular function.

There is a high prevalence of atherosclerotic coronary artery disease in patients with OSA, although it has been debated whether this relationship is cause and effect or simply due to a convergence of common risk factors. Nocturnal ST-segment changes have been previously described in OSA patients, and...
the severity has been reported to correlate with the degree of arterial desaturation. The clinical significance of ST-segment depression in this setting is unclear, and it is currently not known whether OSA may be associated with ST-segment changes in the absence of underlying structural coronary artery disease.

In this issue of CHEST (see page 15), Alonso-Fernandez and colleagues employ very sophisticated biological monitoring techniques to explore the relationship between OSA and cardiovascular disease and attempt to further define potential mechanisms. Their patient population consists of 21 consecutive patients with documented OSA. Polysomnography (which consisted of continuous simultaneous monitoring of the EEG, electro-oculogram, chin electromyogram, and electromyograms of the tibialis anterior muscles bilaterally), oxyhemoglobin saturation, 24-h ambulatory electrocardiograms, and urinary catecholamine determinations were obtained simultaneously in all subjects, and the results were compared with those of 12 snorers without hypersomnia and also with 15 healthy control subjects. Their results are interesting and add to our knowledge of the relationship between cardiovascular disease and OSA.

Compared with the two control groups, OSA patients had more frequent and complex supraventricular and ventricular ectopy as well as a higher incidence of bradyarrhythmias (sinus bradycardia, sinus pauses). Similarly, OSA patients had more frequent episodes of ST-segment depression. Of particular note, 7 of 16 OSA patients had marked ST-segment depression (≥2 mm) compared with no such episodes in the two control groups. These findings correlated in a general way with urinary catecholamine concentrations, sleep fragmentation, and/or nocturnal hypoxemia, although this correlation did not achieve statistical significance in all of the subgroups.

What, if any, are the clinical implications of this information? OSA is more common than is generally realized. The condition clearly leads to considerable morbidity and also excess mortality. If, in addition, OSA is an independent risk factor for cardiovascular disease as has been hypothesized by some, devising preventive strategies may be of paramount importance. The study of Alonso-Fernandez et al provides further evidence of the connection between OSA and cardiovascular disease but falls short of documenting a causative role. One of the limitations of the study is that there is a lack of evidence that any of the ECG abnormalities described by the authors are of any clinical significance. Thus, there is no information about whether the observed ST-segment depression was associated with symptoms that might be attributable to myocardial ischemia (eg, angina in the waking state). Similarly, it is not documented whether any of the patients with arrhythmias during sleep experienced palpitations or syncope while awake. The clinical significance of transient asymptomatic arrhythmias or nocturnal ST-segment depression is unclear. In addition, although patients with known valvular disease, hypertension, or recent myocardial infarction or stroke were excluded from the study, there is no information about risk factors such as dyslipidemia or cigarette smoking or any diagnostic studies such as stress tests, cardiac catheterization, or assessment of left ventricular function. Thus it is difficult to determine the prevalence of organic heart disease within the study population and whether it was comparable between study groups. It also seems unusual that the body mass index in the OSA patients was not significantly different from the other two groups, considering the high prevalence of obesity in OSA. Perhaps, despite the best efforts of the authors, the study population was preselected in a manner that could conceivably have biased the results.

Clearly, more specifically designed prospective trials will be required to clarify the relationship between OSA and cardiovascular disease. Particularly helpful would be large controlled longitudinal studies in which OSA patients undergo initial baseline cardiovascular studies and are followed up prospectively to objective prespecified cardiovascular end points, which are evaluated by a “blinded” events committee. Once the true incidence of various cardiovascular diseases is accurately defined, it will be feasible to initiate follow-up studies to determine whether treatment/prevention of OSA with techniques such as continuous positive airway pressure will be helpful in preventing the development of cardiovascular complications. The cost of such studies, both in resources and actual dollars, will be substantial but may have considerable impact on the incidence of cardiovascular disease.

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Minimally Invasive Is in the Eye of the Beholder

“Big Incisions for Big Operations”

This dictum pervaded surgery for decades. The explosive success of laparoscopic procedures served as a stimulus for seeking smaller windows of access to other body cavities and structures. Old techniques were resurrected, and new technologies were developed as interest surged from both physicians and patients to become minimally invasive. The field of cardiac surgery was not immune to this wave of interest in radically shrinking the size of incisions. Cardiac surgery, particularly coronary artery bypass grafting (CABG), had reached an unparalleled level of success, reliability, and acceptance through the thoughtful blending of cardiopulmonary bypass (CPB) technology, cardioplegic-induced cardiac arrest, enhanced surgical techniques, sophisticated postoperative care, and experience. However, the time was ripe for reassessing what had become the standard approach to surgical revascularization of the heart. The search was begun to seek improvements in the standard CABG operation, which included downsizing the length of the incisions.

The heart is securely guarded in the cage formed by the broad sternal plate and the encircling ribs. The advocacy of the median sternotomy incision by Julian et al in 1957 provided extraordinary access to the heart. No incision has been more effective in exposing the organ targeted for surgery. Longitudinal and complete division of the sternum accomplished several tasks: exposure of the great vessels and heart for cannulation for CPB, unparalleled access to all epicardial coronary arteries, ease of closure, controllable postoperative pain, and the absence of deformity or restriction in activity when healing was completed.

Attempts to perform CABG surgery using CPB and nonsternotomy incisions met with less-than-ideal results. However, the coupling of CPB-supported CABG with partial sternal division has been more successful. This inferiorly placed longitudinal and partial sternal division, accompanied by a transverse sternal incision in the third intercostal space, provided excellent exposure for the epicardial coronary vessels. However, aortic cannulation for CPB and cross-clamping of the aorta were somewhat awkward. Also the “T”-shaped incision lead to bone instability problems. Despite its feasibility, there were sufficient complexities in this approach, when compared to a full sternotomy, that prevented this partial sternal division from becoming the standard of care.

The advent of off-pump CABG (OPCABG) surgery has again prompted interest in reducing the size of surgical incisions. The absence of CPB negated the need to expose the great vessels and atria. The singularly important goal of an incision for an OPCABG procedure was the exposure of the coronary arteries. However, for smaller incisions to replace the standard full sternotomy approach, the abbreviated incisions needed to provide not only equally effective visualization of the coronary arteries, but also demonstrate some measure of superiority: ease of performance, decreased operative time, fewer complications, decreased pain, and/or improved cosmesis.

The article by Niinami et al in this issue of CHEST (see page 47) evaluates an inferiorly placed partial longitudinal sternotomy (without a transverse component) used for single-vessel OPCABG. Although the authors were intending to compare a partial sternotomy with a small anterior thoracotomy, the marked decline in the use of the thoracotomy approach for OPCABG makes isolated evaluation of the partial sternotomy more relevant. This retrospec-

References