Influence of Obstructive Sleep Apnea on Cognitive Impairment in Patients With COPD

To the Editor:

We read with great interest the recent article in CHEST (December 2012) by Villeneuve et al entitled “Mild Cognitive Impairment in Moderate to Severe COPD: A Preliminary Study.” In their article, Villeneuve et al demonstrated that 36% of patients with COPD had mild cognitive impairment (MCI), compared with 12% of healthy subjects. The authors took great care to exclude from the study all patients who presented comorbidities that could affect cognitive function.

With regard to the comorbidities associated with COPD, we would like to highlight the important role of obstructive sleep apnea (OSA). Indeed, it was appreciated by several well-controlled epidemiologic studies that about 20% of subjects with OSA will have COPD, and about 10% of OSA is disclosed among patients with COPD independently of the degree of functional status. There is evidence that OSA has an active role in the development of cognitive impairment. In this regard, in the study of Villeneuve et al, an intriguing finding is the slight (although not significant) increase in the Epworth Sleepiness Scale among patients with COPD and MCI compared with patients with COPD but without MCI, which may lead one to hypothesize the presence of a proportion of patients with OSA among subjects with COPD and MCI.

The primary mechanisms underlying cognitive impairment in OSA are represented by nocturnal hypoxemia, sleep fragmentation, and daytime sleepiness; large studies suggest that hypoxemia is responsible for frontal impairment and executive dysfunction, while sleep fragmentation and daytime sleepiness influence attention. In patients with COPD, hypoxemia, hypercapnia, and vascular comorbidities may be a cause of cognitive alterations. Therefore, in patients with COPD and OSA (overlap syndrome), there is the possibility that all the aforesaid mechanisms operate simultaneously and/or synergistically. In this regard, it is widely accepted that patients with overlap syndrome develop more pronounced, nocturnal, oxygen desaturation than those with COPD or OSA alone. Furthermore, there is evidence that subjects with overlap syndrome show more severe diurnal hypoxemia compared with patients with OSA. For all these reasons, we would like to stimulate discussion about the need to consider the presence of OSA among patients with COPD who have cognitive impairment.

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References

Response

To the Editor:

We thank Dr Damiani and colleagues for their constructive comments on our article in CHEST. They suggested a potential role of obstructive sleep apnea (OSA) in cognitive impairment reported among patients with COPD. It is indeed well established that OSA is associated with cognitive impairment; in fact, OSA was recently described as a risk factor for the development of mild cognitive impairment (MCI) and dementia in elderly individuals. Moreover, a pilot study conducted by our group showed a high frequency of MCI in adults with OSA (38%). This frequency is similar to that which we reported in patients with COPD and is higher than that which we found in healthy subjects (12%).

On the other hand, the prevalence of OSA in patients with COPD has been estimated at 10%, which is similar to that found in an equivalent general population and considerably less than the frequency of MCI observed in our study. OSA is usually diagnosed based on polysonographic recording and the presence of excessive daytime sleepiness. In our study, polysonographic recording was not available to control for OSA. However, based on the Epworth Sleepiness Scale (ESS), patients with COPD did not differ from control subjects in the severity of daytime sleepiness.
symptoms \( (P = .45). \) Although patients with COPD and MCI had a slightly higher ESS total score (8.42) compared with patients with COPD without MCI (6.28), the difference did not reach significance \( (P = .62). \) Furthermore, no significant difference was found in the proportion of subjects with excessive daytime sleepiness \( (ESS \geq 10) \) between patients with COPD and control subjects \( (20\% \text{ vs } 18\%; \chi^2 \text{ test} = 0.02, P = .90) \) or between patients with COPD with and without MCI \( (29\% \text{ vs } 15\%; \chi^2 \text{ test}, P = .41). \) Therefore, although we could not determine the proportion of subjects with objectively confirmed OSA in our sample, our results on the ESS suggest that daytime sleepiness, which is a central symptom in OSA diagnosis, is probably not a major factor explaining the high frequency of MCI in the COPD cohort.

Nevertheless, as mentioned by Dr Damian and colleagues, the coexistence of OSA and COPD (overlap syndrome)\(^1\) may cause more severe cognitive impairment, increasing the risk of cognitive decline in this subgroup of patients. This would have important implications for the clinical support and follow-up of patients with COPD. Thus, further longitudinal studies in larger samples are needed to better assess the impact of OSA on cognition in COPD.

### References


### Antithrombotic and Thrombolytic Therapy for Valvular Disease

**Can This Guideline Apply to Chinese?**

To the Editor:

We were pleased to read the article by Whitlock et al in the February 2012 supplement issue of *CHEST*. They concluded, “In patients with a mechanical mitral valve (both the aortic and mitral position), we suggest [vitamin K antagonist] therapy with a target [international normalized ratio (INR)] of 3.0 (range, 2.5-3.5).” However, we have several concerns about their conclusion.

First, thromboembolism and bleeding while receiving anticoagulants continues to account for 75% of all complications following mechanical heart valve replacement. A significant trend toward a higher frequency of thromboembolism events was observed in the group of non-Chinese patients in Western countries, while the trend in Chinese patients was a higher frequency of bleeding. Hence, there was always doubt as to whether the guideline was appropriate for Chinese patients. This high-intensity strategy is relatively more effective for races other than Chinese. INR levels between 1.5 and 2.0 are recommended for Chinese patients with anticoagulation treatment after mechanical heart valve replacement.\(^3\)

Second, West China Hospital, in Chengdu, has developed a national, multicenter database (Anticoagulation Therapy Database of Chinese Patients After Heart Valve Replacement, unpublished data, January 2011-December 2012) of patients who have undergone heart valve replacement since 2011. The database is part of the Low-intensity Anticoagulation Study. The database is now one of the largest of its kind in China, with 45 centers from 15 provinces participating in the project. To date, detailed information has been collected from >8,000 patients. The preliminary research demonstrates that when INR values are between 1.5 and 2.0, the incidence of both thromboembolic and bleeding complications is the lowest.

Patients in the study need rigorous follow-up. We embarked on this study to establish an anticoagulant guideline that is in accordance with the characteristics of Chinese following heart valve replacement, as well as to provide a potential clinical research tool for the future.

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