Screening for Obstructive Sleep Apnea in Stroke Patients
A Cost-Effectiveness Analysis

Devin L. Brown, MD; Ronald D. Chervin, MD, MS; Susan L. Hickenbottom, MD, MS; Kenneth M. Langa, MD, PhD; Lewis B. Morgenstern, MD

Background and Purpose—Obstructive sleep apnea (OSA) is common after acute ischemic stroke and predicts poor stroke recovery, but whether screening for OSA and treatment by continuous positive airway pressure (CPAP) improves neurological outcome is unknown. We used a cost-effectiveness model to estimate the magnitude of benefit that would be necessary to make polysomnography (PSG) and OSA treatment cost-effective in stroke patients.

Methods—A decision tree modeled 2 alternative strategies: PSG followed by 3 months of CPAP for those found to have OSA versus no screening. The primary outcome was the utility gained through OSA screening and treatment in relation to 2 common willingness-to-pay thresholds of $50,000 and $100,000 per quality-adjusted life year (QALY).

Results—Screening resulted in an incremental cost-effectiveness ratio of $49,421 per QALY. Screening is cost-effective as long as the treatment of stroke patients with OSA by CPAP improves patient utilities by >0.2 for a willingness-to-pay of $50,000 per QALY and 0.1 for a willingness-to-pay of $100,000 per QALY.

Conclusions—A clinical trial assessing the effectiveness of CPAP in improving stroke outcome is warranted from a cost-effectiveness standpoint. (Stroke. 2005;36:1291-1294.)

Key Words: cost–benefit analysis ■ sleep apnea, obstructive ■ stroke management

Obstructive sleep apnea (OSA) is common in ischemic stroke patients and is associated with poor stroke recovery.1,2 It is unknown whether treatment of OSA by continuous positive airway pressure (CPAP) soon after stroke improves neurological outcome. Further, even if CPAP were proven to improve stroke outcome in stroke patients with OSA, screening all stroke patients may not be cost-effective given the costs of polysomnography (PSG). Before a clinical trial is performed to determine the effects of CPAP after stroke, the cost-effectiveness of screening all stroke patients should be determined.

We used a cost-effectiveness model to estimate the magnitude of benefit, in health-state utility, that would be necessary to make PSG and OSA treatment cost-effective in patients with recent stroke. In addition to its usefulness in clinical trial planning, identification of variables that are influential in the model will be informative for cost-reducing strategies.

Methods
The primary outcome was the utility gained through OSA screening and treatment in relation to 2 common willingness-to-pay thresholds of $50,000 and $100,000 per quality-adjusted life year (QALY). Utilities summarize patient preferences for specific health states, ranging from 0 for death to 1 for perfect health. A decision tree (Figure) modeled 2 alternative strategies (screening versus no screening) for a hypothetical adult with recent stroke resulting in a moderate deficit, with an associated health state utility of 0.6. In the screening pathway, identification of OSA led to CPAP titration, followed by 3 months of CPAP treatment. It was assumed that there were no deaths or recurrent strokes over this short time period because these are patients who survived their initial stroke hospitalization.3 The 3-month time horizon also allowed us to assume that no patient in the no-screening arm would come to medical attention due to symptomatic OSA and “crossover” to receive CPAP, thus allowing for a simple model. Reference case estimates of prevalence of OSA and probability of CPAP acceptance in addition to estimated costs and utilities are found in Table 1. The actual short-term acceptance of CPAP in stroke patients is unknown, but this value was allowed to vary in sensitivity analysis. The analysis was performed from a societal perspective using a 3-month time horizon. Costs were estimated based on Medicare reimbursement.4,5 No discounting of costs or utilities was needed given the time horizon. One-way sensitivity analyses were conducted using the ranges found in Table 1. Two-way sensitivity analyses, in which 2 variables were allowed to vary over a plausible range, were conducted with respect to the utility estimates. The decision tree was analyzed by Data 4.0 (TreeAge Inc).

Results
Model results are found in Table 2. In the base case, the incremental cost-effectiveness ratio for screening was $49,421 per QALY. Two-way sensitivity analysis per-
formed on the utilities of stroke states showed that PSG has a cost-effectiveness ratio < $50,000 per QALY as long as the utility for those with OSA on CPAP is ≥0.2 higher than for those with OSA not on CPAP. Therefore, for a willingness-to-pay of $50,000 per QALY, the relative increment in utility would have to be ≥50% (from 0.4 to 0.6), meaning that screening is cost-effective as long as the treatment of stroke patients with OSA by CPAP improves quality of life (QOL) by ≥50%. For a willingness-to-pay of $100,000 per QALY, the relative increment in utility would have to be only ≥25% for screening to be cost-effective.

**Discussion**

This analysis suggests that if CPAP were shown to improve stroke recovery, it would need to improve patients’ utilities by 0.2 in order to be cost-effective given a willingness-to-pay of $50,000 per QALY and by 0.1 for a willingness-to-pay of $100,000 per QALY. In general, interventions that cost < $50,000 to $100,000 per QALY gained are judged to be worthwhile healthcare expenditures. The aforementioned changes in utility represent a 25% to 50% relative improvement in QOL (given the assumption of 0.4 for the utility of a stroke in an OSA patient).

One method for lowering costs associated with PSG screening and CPAP titration would be to attempt to combine the 2 in a split-night study. If the apnea-hypopnea index is ≥20 in the first half of the night, the second half of the night may be used for CPAP titration. This would cut costs considerably to $26,918 per QALY. With the use of a split-night study in all patients, only 16% and 32% improvement in utility would be required to make screening cost-effective given a willingness-to-pay of $100,000 and $50,000 per QALY, respectively.

Another potential cost-saving mechanism would be to use clinical criteria to help identify patients with OSA. Unfortunately, clinical criteria currently identify less than two-thirds of stroke patients with OSA correctly. Therefore, presently, PSG is necessary to screen stroke patients for OSA.

The results of this analysis cannot be extended to those with very mild or very severe strokes. Additionally, this analysis is limited by the validity of the utility estimates used. The utilities used were gathered from patients at risk for stroke given the societal perspective taken. We also performed sensitivity analyses on these values in attempt to compensate for this limitation. Further studies obtaining more precise estimates of QOL and cost information in stroke patients with OSA are needed.

**Summary**

OSA after stroke is common and is associated with poor outcome. A clinical trial assessing the effectiveness of CPAP in improving stroke outcome is warranted from a cost-effectiveness standpoint. The feasibility of performing split-night studies in stroke patients should be assessed as a cost-saving mechanism.

**TABLE 1. List of Percentages, Utilities, and Costs for the Reference Case and Ranges Used for Sensitivity Analyses**

<table>
<thead>
<tr>
<th></th>
<th>Reference Case</th>
<th>Lower Range Tested</th>
<th>Upper Range Tested</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prevalence of OSA in stroke</td>
<td>79%&lt;sup&gt;2&lt;/sup&gt;</td>
<td>50%</td>
<td>80%</td>
</tr>
<tr>
<td>CPAP acceptance</td>
<td>90%&lt;sup&gt;3&lt;/sup&gt;</td>
<td>50%</td>
<td>95%</td>
</tr>
<tr>
<td>Cost of PSG</td>
<td>$800&lt;sup&gt;2&lt;/sup&gt;</td>
<td>$700</td>
<td>$1200</td>
</tr>
<tr>
<td>Cost of CPAP titration</td>
<td>$800&lt;sup&gt;2&lt;/sup&gt;</td>
<td>$700</td>
<td>$1200</td>
</tr>
<tr>
<td>Cost of CPAP plus supplies for 3 months</td>
<td>$457&lt;sup&gt;4&lt;/sup&gt;</td>
<td>$400</td>
<td>$700</td>
</tr>
<tr>
<td>Utility of stroke without OSA</td>
<td>0.6&lt;sup&gt;10&lt;/sup&gt;</td>
<td>0.3</td>
<td>0.8</td>
</tr>
<tr>
<td>Utility of stroke with untreated OSA</td>
<td>0.4&lt;sup&gt;10&lt;/sup&gt;</td>
<td>0.3</td>
<td>0.8</td>
</tr>
<tr>
<td>Utility of stroke with treated OSA</td>
<td>0.6&lt;sup&gt;10&lt;/sup&gt;</td>
<td>0.3</td>
<td>0.8</td>
</tr>
</tbody>
</table>
As Brown et al point out in this issue of *Stroke*, sleep disordered breathing is associated both with increased stroke risk and increased poststroke morbidity and mortality. Obstructive sleep apnea (OSA) is common after stroke, occurring in as many as 60 to 90% of patients, although the natural history of OSA in stroke patients, especially when OSA is first identified during the acute hospitalization, is not well studied. Because effective treatment, namely continuous positive airway pressure (CPAP), is effective at reducing sleep apnea and has been shown in small studies to be feasible in stroke patients, it is reasonable to consider planning trials to evaluate whether CPAP can improve stroke outcomes and reduce subsequent vascular events.

The authors used decision–analytic modeling to identify the magnitude of benefit that identification and treatment of OSA would need to demonstrate to be considered cost-effective. They estimated the magnitude of benefit of screening and treatment of OSA by using quality-adjusted life years (QALYs), a metric that combines one’s preference for a health state with the time that one lives in that health state. They estimated the cost-effectiveness by calculating an incremental cost-effectiveness ratio or the extra costs to screen and treat OSA compared to not screen and treat to gain QALYs. Although the level at which a treatment is considered cost-effective varies, in the US interventions that cost less than $100 000 to $200 000 per QALY are typically considered cost-effective.

As far as decision–analytic models go, this model is simple and thus is missing some elements that would improve its face-validity. The three-month time horizon is simple and thus is missing some elements that would improve its face-validity. The three-month time horizon is not adequately justified, nor is the exclusion of mortality. Important model inputs include the prevalence estimates of OSA, the estimates of acceptance of CPAP, and the estimates of utility of stroke with and without OSA. Although the authors allowed these estimates to vary in sensitivity analyses, the range of estimates in some cases is not adequately justified. As the Cochrane collaboration points out, acceptance of CPAP is almost certainly lower than published studies suggest, so it would be helpful to allow CPAP acceptance to vary below the stated 50% acceptance rate. Importantly, 1 study in a stroke cohort found that only 4 of 34 patients with OSA demonstrated objective compliance with home CPAP over a 3-month period. Key variables that were not directly tested in this model include an estimate of the disutility of testing, and the effect of any reduction in sensitivity or specificity of polysomnography. This is especially important in stroke patients where testing may be done during hospitalization when sleep patterns are already disturbed by the associated environmental and possibly pharmacological milieu. Other treatments for OSA have also been shown to be effective and, in some studies, preferred by patients over CPAP, so including models of other treatment strategies would also be informative. Finally, a 50% increase in utility (from 0.4 to 0.6) associated with treatment may be a somewhat
discouraging target. For example, utility differences for persons with Parkinson disease initially treated with levodopa showed a relative utility increase of only 5 to 10%. Further, although studies typically demonstrate reduction in symptoms with treatment of OSA, this symptom improvement does not always translate to a corresponding improvement in utilities.8,9

When evaluating any model, it is instructive to recall, “All models are wrong, but some are useful.”10 There is no doubt that this model then, like all models, is wrong, but is it useful? We think it so. Not so much in its ability to predict truth or to inform current clinical decision-making, but rather in its approach to technology assessment. This study is an important illustration of the direction we need to move in considering cost-effectiveness modeling in clinical trial planning and ultimately clinical trial conduct. Pilot clinical trial data from studies in OSA could serve to inform not only the precision of the estimates of acceptance and efficacy of CPAP, but also the expected benefit in utility scores, and could allow for evaluation of various methods of assessing patient utilities which may also affect the ability to detect meaningful group differences. Ideally, clinical trial planning groups would include multidisciplinary teams of health economists and quality of life experts to address this critical issue, to ensure that clinical trials will not only address the question of “does this treatment work,” but will also help policy makers and the public with the question of “is the treatment worth the expense?”

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