Upper Airway Stimulation Response in Older Adults with Moderate to Severe Obstructive Sleep Apnea

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Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

Abstract

Objective. To evaluate the impact of age on safety, efficacy, and usage of upper airway stimulation (UAS).

Study Design. Multicenter observational study.

Setting. Thirteen US hospitals and 3 German hospitals.

Subjects and Methods. The ADHERE registry is a multicenter database enrolling patients undergoing UAS implantation from October 2016 to April 2018. Outcome measures included the Epworth Sleepiness Scale, apnea-hypopnea index (AHI), therapy usage, and complications. Data were segmented by age (≤65 vs ≥65 years).

Results. Younger adults (n = 365) were a mean ± SD 52.7 ± 7.9 years old and 82% male, with a body mass index of 29.6 ± 3.8. Older adults (n = 235) were 71.1 ± 4.8 years old and 71% male, with a body mass index of 28.8 ± 3.8. Baseline AHI was similar (younger, 36.2 ± 15.9; older, 36.1 ± 14.8). Both groups had lower AHI at 12 months versus baseline (P < .001), but the older group showed a greater reduction (7.6 ± 6.9 vs 11.9 ± 13.4, P = .01). The Epworth Sleepiness Scale score decreased from 12.3 ± 5.4 to 7.1 ± 4.8 (P < .001) among younger adults and from 10.7 ± 5.7 to 6.3 ± 4.4 (P < .001) among older adults. Usage was slightly higher among older adults (6.0 ± 2.0 vs 5.4 ± 2.1 hours/night, P = .02). Surgical time was similar between younger patients (2.4 ± 0.7 hours) and older patients (2.3 ± 0.7 hours, P = .40), with comparably low complications.

Conclusion. AHI reduction and therapy usage were found to be somewhat higher among patients aged ≥65 years who were treated with UAS. Surgical complications were low, in contrast to traditional sleep surgery.

Keywords upper airway stimulation, obstructive sleep apnea, CPAP intolerance, hypoglossal nerve stimulator, inspire therapy, sleep surgery, geriatric sleep

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Obstructive sleep apnea (OSA) remains a significant disease, affecting roughly 30 million Americans. It is associated with an increased risk of cardiovascular and cerebrovascular disease and is a significant socioeconomic burden due to productivity loss and health care–associated costs.1 The gold standard of care for OSA is continuous positive airway pressure (CPAP) therapy; however, problems of noncompliance and poor adherence plague this treatment modality. A meta-analysis from 2016 identified 82 high-quality studies addressing CPAP tolerance and determined an overall nonadherence rate of 34.1%. Additionally, they reported a mean 4.6 hours of nightly use, below the accepted 5- to 6-hour nightly requirement necessary to achieve the optimal benefit of CPAP therapy.2 These issues highlight the need for low-morbidity, highly effective treatment options for patients who are CPAP intolerant.

In 2014, the Food and Drug Administration approved the first hypoglossal nerve stimulator for the treatment of OSA (Inspire Medical Systems, Maple Grove, Minnesota). This therapeutic modality is often referred to the moniker upper airway stimulation (UAS) due to the more diffuse, global effects produced on the upper airway. This surgically implanted device combats the underlying hypotonia seen in OSA by coupling respiratory effort with upper airway muscle stimulation. The STAR trial found UAS to be highly efficacious, with a median 68% decrease in apnea-hypopnea index (AHI) severity.3 Since its approval, UAS has become a well-tolerated and widely adopted tool in the sleep surgeon’s

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armamentarium. Accordingly, numerous studies have since confirmed and expounded on the efficacy initially reported in the STAR trial.\(^4\) Interestingly, a recent 5-year analysis of the STAR cohort suggested that older adults might exhibit a more robust response than younger adults following UAS.\(^5\)

As Gouveia et al pointed out,\(^6\) the population \(>65\) years old is the fastest growing in the United States; with an increasing incidence of OSA, novel treatments must be determined to be safe and efficacious in this expanding population. Few studies to date have addressed varying treatment responses to sleep surgery based on age, and those that have done so suggested a poorer response among older patients as compared with younger patients.\(^7,8\)

The goal of our study was to demonstrate that UAS is a highly effective treatment modality for qualified patients \(\geq 65\) years of age, using data from the ADHERE registry (Adherence and Outcome of Upper Airway Stimulation for OSA International Registry).\(^9\) The ADHERE registry is a multicenter prospective cohort open to all UAS-implanting programs that have the clinical research capacity to support data collection and follow-up from the time of implant to 1 year postoperatively, and it represents 600 of the 3000 patients who have been treated with UAS to date. We report the objective and subjective therapy efficacy, adherence, procedural length, complications, and patient-reported outcomes for patients \(<65\) and \(\geq 65\) years.

**Methods**

**Study Design**

The ADHERE registry is an ongoing multicenter observational study enrolling patients who received UAS therapy (Inspire Medical Systems), to collect evidence of safety and efficacy in a standard clinical practice setting. The registry began enrollment in October 2016 and, at the time of this analysis, continues across 13 sites in the United States and 3 in Germany. Inclusion criteria were moderate to severe OSA (AHI, 15-65), \(<25\%\) central and mixed apneas, CPAP nonadherence or intolerance, absence of concentric collapse during sleep endoscopy, and implantation of the UAS device. The study design followed standard of care, and there were no additional tests or interventions.

The UAS device was implanted with visit schedules as previously described.\(^9,12\) Following implantation, the device remained off until programming approximately 1 month after implantation, followed by a 2- to 6-month device check and postimplant polysomnography and, according to local clinical practice, a 12-month postimplant follow-up device check and polysomnography or home sleep study.

The study was approved by each hospital’s institutional review board or ethics committee. All patients provided informed consent, and data were retrieved from the medical records. The study is registered as NCT02907398 on clinicaltrials.gov.

**Outcome Measurements**

Baseline measurements prior to implant included patient demographics and sleep apnea history. Operative outcomes included surgical time and postoperative adverse events. Sleep apnea outcomes at each visit interval included the AHI, Epworth Sleepiness Scale (ESS), and objective therapy usage as reported by the device. Therapy satisfaction, as reported by the clinician, was measured with the Clinical Global Impressions Scale, and patient satisfaction was measured with the Net Promoter Score.\(^13\)

**Statistical Analysis**

Data from all enrolled patients from October 2016 through April 2018 were analyzed for this report. The data were stratified by age. Younger adults were defined as \(<65\) years old and older adults as \(\geq 65\) years. The outcome measurements were compared between the groups with the same visit intervals. Statistical significance was determined with the Student \(t\) test, and \(P\) values \(<.05\) were considered statistically significant. Results are presented as mean ± SD.

**Results**

Among the 600 patients from the registry, 61% were \(<65\) years old, and 39% were \(\geq 65\) years. The patients were predominantly male, Caucasian, and with relatively few comorbidities—mainly hypertension (7\%), depression (3\%), diabetes mellitus (1\%), and atrial fibrillation (1\%). The older and younger groups had a similar baseline AHI; however, older adults had lower body mass index (BMI; 28.8 ± 3.8 vs 29.6 ± 3.8, \(P = .02\)) and were slightly less sleepy per the ESS (10.7 ± 5.7 vs 12.3 ± 5.4, \(P < .001\); Table 1).

The operative time was similar between the groups. The mean surgical time was 2.4 ± 0.7 hours for younger patients and 2.3 ± 0.7 hours for older patients (\(P = .40\)). Implant-related adverse events occurred among 3\% of younger patients and 1\% of older patients.

Younger and older patients both had a significant AHI reduction when compared with baseline; however, older patients had a larger therapeutic reduction in AHI after 1 year (−28.1 ± 14.4 vs −22.2 ± 18.2, \(P = .01\); Figure 1). The ESS score decreased by similar amounts in both groups, despite a lower baseline ESS score among older patients.

In both groups, therapy usage exceeded the commonly used criteria for CPAP tolerance of 20 hours per week.\(^14\) Notably, older patients demonstrated slightly higher therapy usage at posttitration and 12-month follow-up than younger patients (Figure 2).

The older group had higher Clinical Global Impressions Scale scores and was more likely to recommend UAS to friends and family than the younger patient group. The clinician global impression for the younger group was 93.6\% improvement at the posttitration visit and 91.8\% at the 12-month visit. Clinicians reported a higher proportion of improvement in the older group, with 97.8\% showing improvement at posttitration and 98.7\% at the 12-month visit (Figure 3).

Patient-reported scores also illustrated this phenomenon. The younger group reported 90.6\% agreement that it would recommend UAS to friends and family at posttitration,
increasing to 93.4% at the 12-month visit. In the older group, 97.0% of patients agreed that they would recommend the UAS to friends and family, which increased to 97.7% at the 12-month visit (Figure 4). No major adverse events occurred (Table 2).

**Discussion**

Our study was designed to assess the hypothesis that UAS is a highly effective treatment modality for qualified patients ≥65 years of age, as well as to evaluate the potential for a more robust treatment response in this age group as reported by Woodson et al.5 As the definition of CPAP therapeutic success for the treatment of sleep apnea is defined by Medicare (the primary insurer of those ≥65 years of age), we utilized an age cutoff of 65 years for our study. In our study, both the younger and older groups showed a significant response to therapy, although the response was somewhat greater in the older population. Subgroup analysis of patients aged 65 to 74 years and ≥75 years failed to demonstrate a difference (Table 3).

A recent analysis concerning the primary physiologic factors contributing to OSA suggested that older patients might have distinctly different physiologic phenotypes than...
younger patients. The authors reported that older patients tend to exhibit greater upper airway collapsibility as well as reduced ventilatory demand as compared with younger patients. These findings would suggest that UAS, with its subsequent increase in upper airway muscle tone, may be a well-suited treatment option in this patient population. Additionally, such findings might account for previous reports of poorer outcomes with traditional sleep surgery among older patients.

ESS scores provide further evidence supporting the efficacy of UAS for older patients. In a recent study of patients aged 65 years old, McMillan et al reported a 2-point reduction in ESS 12 months after CPAP initiation, as compared with a nearly 5-point reduction seen in a comparable population treated with UAS. In addition, our study demonstrated that therapy usage was higher in the older population than in younger population, with both groups being higher than previously reported average nightly CPAP usage. Although the exact reason for the increased usage among older patients is unclear, it is possible that this reflects an increased total sleep time among older patients who are largely retired as compared with younger patients who might have additional work/life responsibilities.

Gouveia et al reported that age was an independent predictor of postsurgical complications among patients undergoing multilevel sleep surgery. Since its Food and Drug Administration approval, UAS has been lauded as a dramatically less morbid alternative to other surgical procedures used to treat OSA. Our study reaffirmed the excellent safety profile of UAS and found no significant difference in complication rates between the younger and older cohorts. It is worth noting that our population exhibited comorbidities

**Figure 3.** Clinical Global Impressions Scale scores at first postoperative titration visit and 12-month follow-up between younger and older age groups.

**Figure 4.** Net Promoter Scores at first postoperative titration visit and 12-month follow-up between younger and older age groups. UAS, upper airway stimulation.

**Table 2.** Implant-Related Adverse Events.

<table>
<thead>
<tr>
<th>Implant-Related Adverse Events</th>
<th>Younger Patients (n = 10, 3%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intraoperative bleeding requiring additional suture or electrocautery</td>
<td>2a</td>
</tr>
<tr>
<td>Seroma</td>
<td>2</td>
</tr>
<tr>
<td>Temporary tongue weakness or dysarthria</td>
<td>2</td>
</tr>
<tr>
<td>Hematoma</td>
<td>1</td>
</tr>
<tr>
<td>Submandibular swelling</td>
<td>1</td>
</tr>
<tr>
<td>Bleeding related to nasal anesthesia</td>
<td>1</td>
</tr>
<tr>
<td>Displaced stimulator cuff</td>
<td>1</td>
</tr>
</tbody>
</table>

*a*Older patients, n = 2 (1%).

**Table 3.** Subgroup Analysis of Therapeutic Response: Patients Aged 64-74 vs ≥75 Years.

<table>
<thead>
<tr>
<th></th>
<th>65-74 y</th>
<th>≥75 y</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Entries, n</td>
<td>173</td>
<td>59</td>
<td></td>
</tr>
<tr>
<td>AHI</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>36.5 ± 15.1</td>
<td>35.4 ± 14.1</td>
<td>.57</td>
</tr>
<tr>
<td>Posttitration</td>
<td>9.2 ± 11.9</td>
<td>9.3 ± 10.6</td>
<td>.97</td>
</tr>
<tr>
<td>Change</td>
<td>−28.1 ± 17.1</td>
<td>−25.8 ± 14.5</td>
<td>.43</td>
</tr>
<tr>
<td>12 mo</td>
<td>7.7 ± 7.4</td>
<td>7.7 ± 5.0</td>
<td>.99</td>
</tr>
<tr>
<td>Change</td>
<td>−28.5 ± 15.0</td>
<td>−26.9 ± 12.7</td>
<td>.67</td>
</tr>
</tbody>
</table>

Abbreviation: AHI, apnea-hypopnea index.
corresponding to those of the patients undergoing multilevel sleep surgery.

The true test of time for UAS will be whether it is associated with decreased mortality and reduction of health risks (e.g., cardiovascular). Prior studies addressing the effect of CPAP on cardiovascular mortality had conflicting data, with some demonstrating reduced hazard ratios and other not. The latter studies were typically confounded by poor CPAP adherence.\textsuperscript{14,17} One could reasonably argue that the high efficacy and improved patient adherence seen with UAS could lead to a reduction in the negative health consequences of untreated OSA. Long-term follow-up of greater numbers of patients treated with UAS will be necessary to confirm the validity of such an assertion.

One limitation worth noting is the significance of BMI in our older patient population. We recognize BMI as a confounding predictor of therapy outcome with age, especially given the lower BMI of the older group versus the younger group. As this report compares therapy outcomes between older and younger patients, it is likely that age and BMI are both associated with the therapeutic outcome of UAS.

We feel strongly that the results of our study confirm that UAS represents an excellent treatment in well-selected CPAP-intolerant cases of OSA, including those aged \( \geq 65 \) years. Dysphagia can be seen with increasing prevalence among older patients, often related to other comorbidities. Unlike traditional sleep surgery, which is associated with varying degrees of negative impact on swallowing, UAS does not permanently alter the upper aerodigestive tract and thus has no such detrimental effects. Consistent and durable improvement coupled with the extremely low morbidity of the procedure makes it a reasonable option even among less robust elderly patients in need of a treatment alternative to CPAP.

**Conclusion**

This study corroborates the growing evidence supporting the safety and efficacy of UAS for the treatment of OSA in properly selected CPAP-intolerant cases. In addition, it affirms the benefit of UAS for older patients, who were previously shown to have worse outcomes with other types of sleep surgery. It is noteworthy that age \( \geq 65 \) years is an independent factor for success with UAS as compared with younger cohorts. UAS should be strongly considered in the treatment of older patients who are CPAP intolerant and eligible per established inclusion criteria.

**Author Contributions**

Kirk Withrow, conception, acquisition and analysis of data, drafting and final approval of manuscript, Sean Evans, acquisition and analysis of data, revising and final approval of manuscript, John Harwick, conception, acquisition and analysis of data, drafting and final approval of manuscript, Eric Kezirian, acquisition and analysis of data, revising and final approval of manuscript, Patrick Strollo, conception, acquisition and analysis of data, revising and final approval of manuscript.

**Disclosures**

**Competing interests:** Eric Kezirian—Inspire Medical Systems (honoraria, research funding); Pillar Palatal, Nyxoah, CryOSA, Split Rock Scientific, Gerard Scientific, Berendo Scientific (scientific advisory board, consultant); Magnap (intellectual property rights); Patrick Strollo—Inspire Medical Systems (honoraria, research grant, consultant); Jazz Pharmaceuticals (research grant, advisory board); ResMed, Philips Respironics (research grant, consultant).

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**References**


