Comparison of clinical pathways for hypoglossal nerve stimulation management: in-laboratory titration polysomnography versus home-based efficacy sleep testing

Hypoglossal nerve stimulation (HNS)

- HNS therapy is an alternative treatment option for patients with obstructive sleep apnea who are intolerant to positive airway pressure therapy.

- Therapy adjustments are typically completed during in-laboratory titration polysomnography (tPSG) after approximately 3 months of patient HNS self-titration at home.

Titration

- The standard of care for HNS titration and efficacy assessment is tPSG, but has certain limitations
  - High cost
  - Geographic distance
  - Resource limitations, and comfort with the laboratory environment

- Home sleep apnea testing (HST) mitigates some of these issues due
  - Less burdensome equipment
  - Lower cost
  - Ability for patients to sleep in their home environment

- HST has never been directly compared to tPSG to determine whether one results in more effective therapy outcomes for patients

➢ Methods

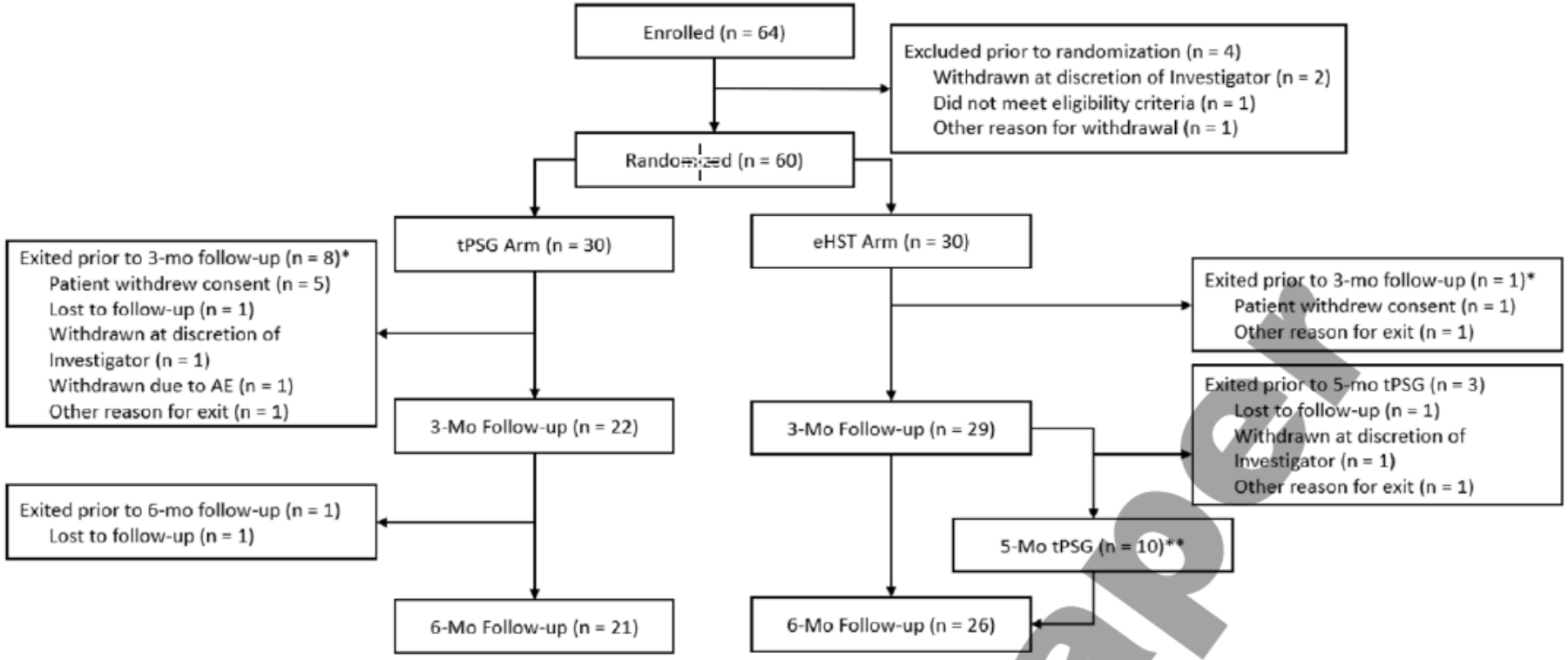
- Prospective, randomized, non-blinded, multi-center trial across 5 centers in the United States evaluating two different care pathways of HNS titration with endpoints evaluated 6 months after therapy activation

- Sixty-four patients were enrolled who underwent unilateral HNS device implantation and were randomized on a 1:1 basis between two post-implant management arms at the 1-month postoperative activation visit.

- The control arm underwent tPSG at 3-months post-activation as per current standard of care. The home monitoring arm underwent a 2-night HST at the 3-month post-activation visit.

- The 3-month HNS responder status was determined using the Sher15 responder criteria (AHI < 15 events/h and ≥50% reduction from baseline)

Study enrollment, randomization, and attrition



*Patients may have had more than one reason for study exit.

**One patient missed the 5-month tPSG but completed the 6-moth follow-up visit.

➢ Results

- Patients were similar between two arms, comprised of predominantly older, male Caucasians with severe OSA diagnosed primarily via HST. Ultimately, 70% completed the tPSG arm, and 87% completed the HST arm

- The 6-month AHI was statistically equivalent between two arms, with a median of differences of -0.23 events/h

- The mean 6-month post-activation AHI with HNS therapy was 13.5 events/h in the tPSG arm, and 14.6 in the HST arm, with a mean difference of -0.01 events/h, again demonstrating statistical equivalence.

- There were no significant differences between the tPSG and eHST arms by Sher15 or Sher20 responder rates at 6 months

Table 1—Baseline characteristics (mean ± SD) by randomization arm.

Patient Characteristics	tPSG	eHST	All Patients	*P*
n	30	30	60	
Age (years)	58.07±10.11, n=30	54.23±10.89, n=30	56.15±10.6, n=60	0.16
Sex				
Male, %	53.3%	76.7%	65.0%	0.10
Female, %	46.7%	23.3%	35.0%	
White, %	96.7%	100.0%	98.3%	1.00
BMI (kg/m^2)	28.69±3.12, n=30	29.2±3.78, n=30	28.95±3.45, n=60	0.57
Baseline				
AHI (events/h)	35.13±19.14, n=30	35.02±14.46, n=30	35.08±16.81, n=60	0.98
ODI (events/h)	29.95±25.18, n=24	30.65±20.08, n=22	30.29±22.64, n=46	0.92
ESS	9.96±5.58, n=25	9.75±6.58, n=28	9.85±6.07, n=53	0.90
Baseline sleep test				
HST, %	56.7%	80.0%	68.3%	0.09
PSG, %	43.3%	20.0%	31.7%	
Baseline comorbidities				
Sleep (other than OSA)	10.0%	16.7%	13.3%	0.71
Cardiovascular	46.7%	36.7%	41.7%	0.60
Neurologic	13.3%	6.7%	10.0%	0.67
Psychiatric	36.7%	46.7%	41.7%	0.60
Endocrine	23.3%	26.7%	25.0%	1.00
Other conditions	40.0%	30.0%	35.0%	0.59

See supplemental material for diagnoses matching baseline comorbidity categories. tPSG = in-laboratory titration polysomnography; eHST = efficacy home sleep apnea test; BMI = body mass index; OSA = obstructive sleep apnea; AHI = apnea-hypopnea index; ODI = oxygen desaturation index; ESS = Epworth Sleepiness Scale.

Table 2—Equivalence in 6-month apnea-hypopnea indices (AHI) and change in AHI from baseline between randomization arms.

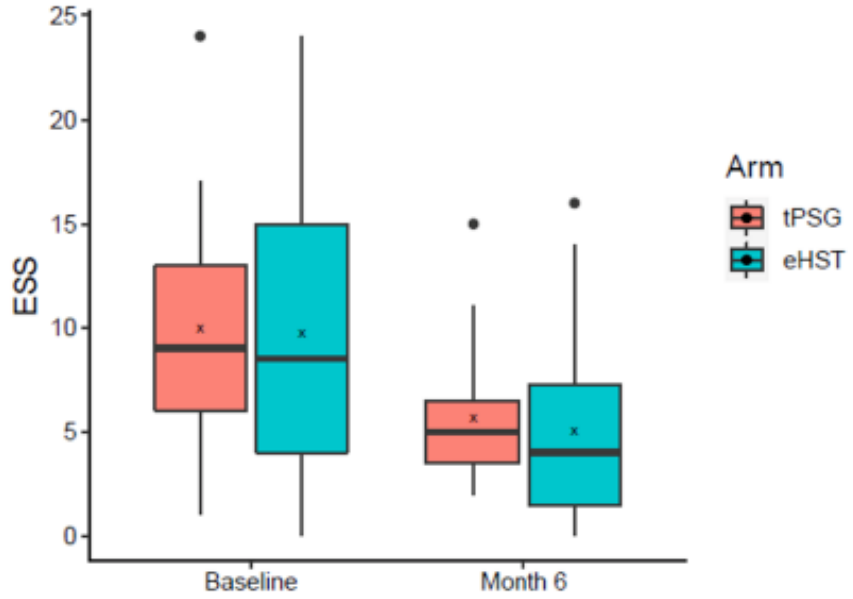
Endpoint	tPSG	eHST	Estimate	95% CI	Equivalence Margin
6-month AHI	13.49 [7.75, 19.23], n=19	14.62 [8.41, 20.83], n=22	-0.23	-6.2, 4.2	-15, 15
6-month Change in AHI	-21.89 [-28.33, -15.45], n=19	-21.89 [-29.75, -14.03], n=22	-0.01	-8.75, 8.74	-15, 15

Table 3—6-month responder rate per $Sher_{15}$ and $Sher_{20}$ criteria by

Variable	tPSG	eHST	*P*
n	19	22	
$Sher_{15}$ criteria			
Responder	63.2% (12)	59.1% (13)	1
Non-responder	36.8% (7)	40.9% (9)	
$Sher_{20}$ criteria			
Responder	68.4% (13)	63.6% (14)	1
Non-responder	31.6% (6)	36.4% (8)	

Responder rates were compared using Fisher's Exact Test.

Figure 2—Baseline and 6-month Epworth Sleepiness Scale (ESS) by randomization arm.



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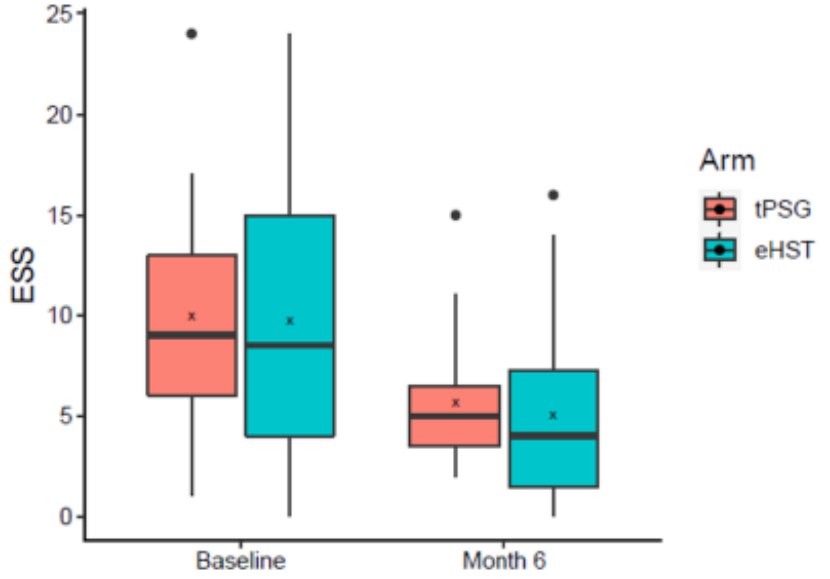

➢ Results

- Six-month Epworth Sleepiness Scale was 5.7 for the tPSG arm and 5.0 for the HST arm, but statistical equivalence was not met as the confidence interval of the median of differences crossed the 2-point equivalence margin.

- Oxygen Desaturation Index was 11.6 events/h in tPSG versus 13.6 events/h in HST and was statistically equivalent.

- Therapy usage at 6 months was similar between the two arms (6.1 hours/night each), but the confidence intervals of the median of differences did not meet the equivalence margin

Table 4 —Equivalence in 6-month Epworth Sleepiness Scale (ESS), oxygen desaturation index (ODI), and therapy usage between randomization arms.

Endpoint	tPSG	eHST	Median of Differences	Confidence Interval	Equivalence Margin
ESS equivalence	5.68 [4.23, 7.13], n=19	5 [2.87, 7.13], n=20	1.00	-1, 3	-2, 2
ODI equivalence	11.57 [7.35, 15.79] n=19	13.57 [8.81, 18.33] n=22	-0.85	-7.4, 4.4	-15, 15
Therapy usage (h/night) equivalence	6.1 [5.09, 7.11] n=21	6.1 [5.35, 6.85] n=26	0.00	-1.29, 1.29	-0.5, 0.5

Data presented as mean [95% CI]. Median of differences (location shift) and confidence interval derived using non-parametric Hodges-Lehmann test.

➢ Discussion

- This prospective, multicenter, randomized clinical trial demonstrated that
  - ➢ Patients self-titrating HNS therapy with periodic home-based efficacy assessments experienced equivalent decreases in objective measures of OSA burden to patients undergoing active laboratory-based adjustments.
  - ➢ HST patients experienced similar overall response rates to therapy and experienced similar improvements in ODI.
- The findings suggest that most patients can effectively adjust HNS therapy in the home setting according to subjective experience and comfort to achieve substantive objective decreases in OSA burden.
- Both study arms additionally had similar mean amplitude levels at the 3- and 6-month visits.

➢ Conclusion

- These findings indicate that tPSGs may not provide substantial benefit over HST monitoring during the initial HNS titration process, as most responders achieved success through straightforward increases in amplitude.

➢ Limitations

- Use of both 2012 hypopnea scoring rules in the preoperative sleep studies
- Predominantly white and of low BMI
- Primary endpoint at 6 months after therapy activation instead of the more commonly observed 12-month
- 3-month eHST non-responders to tPSG at 5 months, while the tPSG arm non-responders were not required to undergo tPSG
- Almost a third of the patients assigned to tPSG exited the study prior to the 3-month in-laboratory assessment.

