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COMMENTARY

Large telemonitoring databases: the good, the bad, and the useful

Commentary on Malhotra A, Benjafield AV, Cistulli PA, et al. Characterizing respiratory parameters, settings and adherence in real-world patients using adaptive servo ventilation therapy: big data analysis. *J Clin Sleep Med*. 2021;17(12):2355–2362. doi:10.5664/jcsm.9430

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In this issue of the *Journal of Clinical Sleep Medicine*, Malhotra et al[1] have yet again taken advantage of a large cloud-based telemonitoring database, this time to provide insights into the "real world" usage of adaptive servo-ventilation (ASV) devices.[1–3] Their main objective in this recent work[1] was to address questions that remain following publication of the SERVE-HF trial,[4] but I think we learn other important things along the way.

The SERVE-HF trial found increased mortality in patients with heart failure and reduced ejection fraction (HFrEF) who received ASV therapy for central sleep apnea (CSA) compared with those receiving best medical care alone.[4] This was an unexpected result, and many explanations have been offered.[5] A contested hypothesis that CSA is a compensatory and protective mechanism that we ought to be reluctant to treat has been offered.[6,7] Others have suggested that flaws in the design, execution, and data collection biased results.[5] Finally, many have raised concerns about how the device used in the trial may have done an inadequate job of controlling the sleep-disordered breathing and may have led to hyperventilation, which in turn may have led to the undesired results.[5,8] Specifically, the device used in the SERVE-HF trial provided a fixed end positive airway pressure (EPAP) that was set relatively low (95th percentile was < 6 cm of water, or CWP), raising concerns that there may have been times when obstructive events were inadequately suppressed. This concern is buoyed by the relatively elevated residual apnea-hypopnea index (AHI), which averaged between 6.2–6.7 events/h, and ranged as high as 50 events/h. Since the device would register the resultant apneas or decline in minute ventilation (VE), the servomechanism would increase pressure support, resulting in increased intrathoracic pressures and/or increased VE. Another concern was that delivery of a minimum pressure support (PSmin) of 3 may have driven VE excessively high. The combinations of higher intrathoracic pressure leading to reduced cardiac output along with hyperventilation leading to arrhythmogenic alkalosis may have contributed to the worse outcomes. Malhotra et al sought to use a large telemonitoring database to determine if there was a relationship between EPAP or PS and VE or peak pressures.

With these concerns in mind, their study had several main findings. First, PSmin had no clinically significant effect on VE or respiratory rate over a wide range of PSmin. This suggests that the previously raised concerns that PSmin drove excessive VE may be unfounded. Secondly, average median VE was similar in patients using a fixed EPAP and those with an auto-adjusting EPAP. This suggests that the prior hypothesis that low EPAP may have led to increased PS with resultant hyperventilation should be rejected, but we cannot really conclude that because fixed EPAP and autoEPAP settings were similar and higher than in the SERVE-HF study (median 8.0 ± 2.5 CWP in this study vs 5.5–6.1 CWP in the SERVE-HF trial).[1,4] It is unfortunate that we do not have actual VE data from the SERVE-HF trial that could be compared with this more contemporary dataset.

Mining large telemonitoring databases provides some advantages.[2,3] In this instance we have data from nearly 64,000 patients, allowing evaluation of a wide range of ASV settings over a long time with significant statistical power. The large dataset helps us understand what to expect for pressures, leak, residual AHI, and adherence over broad populations using it in real life.[2] However, there are also significant limitations. Because it is observational, we learn only about those who have access to and use this therapy. Since nearly a quarter of patients who are given a prescription for PAP never start using it, this almost certainly biases the study population.[9] These data provide no demographic, diagnostic, or comorbidity information, and therefore represent a heterogeneous population. We can't make any secure inferences about what, for example, the mean EPAP or PS settings are or what the VE or AHI measures are for patients with HFrEF and CSA. We simply don't know. Because of this, I'm not sure that these data shed as much light on the concerns about SERVE-HF as we would like.

However, these new data tell us some important practical things. In our practice, we should expect higher adherence than has been seen in many of the clinical trials (eg > 6 h/d in Malhotra et al vs 3.4 h/d in the SERVE-HF trial), perhaps because we treat patients who are more symptomatic or because patients receive better support in clinical practice.[10] Previously, I often would begin ASV treatments with PSmin at 3 CWP, PSmax at 15 CWP, and adjust these only when I encountered difficulties during PSG

or in follow-up. These new data suggest that I should consider setting the PS based upon the patient's breathing comfort right from the beginning, perhaps beginning with a PSmin of 0 CWP, without a priori expectation that this will significantly affect the delivered VE. These data provide new information to guide assessments during follow-up. A residual AHI of around 5 events/h is associated with higher adherence than when the residual is 10 events/h, even perhaps at the risk of using a higher EPAP or inspiratory positive airway pressure (IPAP), because higher pressures were not associated with worse adherence. The data also suggest we ought to pay significant attention to reducing leak, perhaps targeting a median leak less than 4 L per minute.

Large telemonitoring databases do provide useful information, but they can't answer certain questions as they are currently configured. However, we will be able to learn so much more as we find the ways to combine real-world observational data with user-specific clinical data, all while preserving needed privacy.[11]

CITATION

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REFERENCES

1. Malhotra A, Benjafield AV, Cistulli PA, et al. Characterizing respiratory parameters, settings and adherence in real-world patients using adaptive servo ventilation therapy: big data analysis. *J Clin Sleep Med*. 2021;17(12):2355–2362.
2. Cistulli PA, Armitstead J, Pepin J-L, et al. Short-term CPAP adherence in obstructive sleep apnea: a big data analysis using real world data. *Sleep Med*. 2019;59:114–116.
3. Pépin J-LD, Woehrle H, Liu D, et al. Adherence to positive airway therapy after switching from CPAP to ASV: a big data analysis. *J Clin Sleep Med*. 2018;14(1): 57–63.
4. Cowie MR, Woehrle H, Wegscheider K, et al. Adaptive servo-ventilation for central sleep apnea in systolic heart failure. *N Engl J Med*. 2015;373(12):1095–1105.
5. Javaheri S, Brown LK, Randerath W, Khayat R. SERVE-HF: more questions than answers. *Chest*. 2016;149(4):900–904.
6. Naughton MT. Cheyne-Stokes respiration: friend or foe? *Thorax*. 2012;67(4): 357–360.
7. Javaheri S. CPAP should not be used for central sleep apnea in congestive heart failure patients. *J Clin Sleep Med*. 2006;02(4):399–402.
8. Floras JS, Logan AG, Bradley TD. Adaptive servo ventilation for central sleep apnea: more data, please. *Can J Cardiol*. 2016;32(3):396.e3.
9. Lin H-S, Zuliani G, Amjad EH, et al. Treatment compliance in patients lost to follow-up after polysomnography. *Otolaryngol Head Neck Surg*. 2007;136(2): 236–240.
10. Pack AI, Magalang UJ, Singh B, Kuna ST, Keenan BT, Maislin G. Randomized clinical trials of cardiovascular disease in obstructive sleep apnea: understanding and overcoming bias. *Sleep*. 2021;44(2):zsaa229.
11. Kurian T. How Google and Mayo Clinic Will Transform the Future of Healthcare. https://cloud.google.com/blog/topics/customers/how-google-and-mayo-clinic-will-transform-the-future-of-healthcare. Accessed October 1, 2021.

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The author has seen and approved the final manuscript and reports no conflicts of interest.