Received: 20 June 2022 | Accepted: 11 July 2022

DOI: 10.1111/resp.14332

EDITORIAL

Official Journal of the Asian Pacific Society of Respirology
Respirology
APSR
WILEY

Endotyping in sleep surgery: Not ready for primetime

In most adults, the recommended first-line therapy for moderate to severe obstructive sleep apnoea (OSA) is continuous positive airway pressure (CPAP) therapy. However, in a real-life context, many adults with OSA struggle to tolerate CPAP. Over the last decade, researchers have targeted 'methodologies of prediction' to determine the potential benefits of salvage therapies such as mandibular advancement splints (MAS), upper airway surgery, medications, weight loss and even myofunctional therapies.

The recent publication by Wong et al.[1] in *Respirology* explores the possibility of utilizing endotypic features in the prediction of adult OSA surgery outcomes. This research is unique in assessing how upper airway surgery influences all four PALM-defined endotypes,[2] employing two different methodologies (CPAP dial-down and polysomnography-derived). The authors are to be congratulated for such an original publication.

The authors found that whilst upper airway surgery can improve collapsibility, no non-anatomical endotype permitted the prediction of outcomes. One conclusion might be that evaluating endotypes alone is not as useful as deciding clinically upon whom to operate. This is opposed to other treatments such as MAS where endotyping predicted outcomes, based on similarly structured research into those therapies.

However, despite the authors' excellent work, several key questions remain unanswered.

First (and most notably), if the recorded anatomical/dynamic assessment findings were married with physiological endotypes, could outcomes have been predicted?

In clinical practice, the site and pattern of upper airway collapse defined during examination is currently recommended as the most important determinant in selecting which customized surgical procedure to perform. Wong et al. dedicatedly recorded site and degree of collapse at dynamic nasendoscopy but it would have been interesting to see if these assessments when married with the endotypes led to a change in the surgical procedure that was performed. Nearly a third of patients in the study had circumferential collapse, mostly to a large degree, but still received surgery. Some of these had such collapse recorded at levels at which it may not occur, based on recognized scoring systems.[3] Even those who collapsed in an Antero-Posterior or lateral pattern did not necessarily receive a surgical technique that is thought to control or improve those specific planes of collapse.[4] Wong et al. suggested there are 'no reliable (anatomical) predictors of response' in surgery, although there is a growing body of literature regarding tonsil size,[5] Friedman stage,[6] Drug Induced Sleep Endoscopy and dynamic predictors[7] (albeit with argument about reproducibility) and accepted algorithms.[8] Future research integrating preoperative anatomy (static and dynamic) with endotyping might either generate different predictability outcomes or allow more robust conclusions about findings to be drawn.

Second, could the emphasis on supine non-rapid eye movement measures have negated the fact that some surgical literature demonstrates more reliable apnoea–hypopnoea index (AHI) and symptom improvement in the more common lateral position of sleep[9]?

The answer to this question is unknown. Furthermore, supine sleep during polysomnography may be 'over-represented' as patients struggle with multiple leads and attachments. Conversely, CPAP therapy, if worn, tends to control apnoea and hypopnoea in all positions.

Third, if definitions used for 'responders' by Wong et al. were commensurate with those in the surgical literature, would different results be seen?

The authors clearly defined 'responders' but did so a little differently to those accepted in the surgical literature.[10] Inter-linked is the authors' noting 'many patients have residual OSA post-surgery'—even though the referenced articles included patients who underwent surgery and had residual hypopnoea only, with large symptom improvement.[11] Given so many patients have derived symptomatic benefit from salvage surgery in the referenced papers, residual hypopnoea may have limited meaningful clinical impact. Potentially assessing the apnoea index and oxygen desaturation outcomes without hypopnoea might carry more weight and offer preferable targets for assessing methodologies of prediction.

Fourth, could a larger sample size have yielded different results?

Whilst the authors executed an excellent physiological study, sample size modelling based on single (upper airway collapsibility = 18) or dual endotypes (LG and arousal threshold = 7–21) may not be adequate to provide an 'all four endotypes sample size' the authors targeted. Larger studies across multiple sites might permit greater validity in determining the value (or lack thereof) of endotyping surgical candidature. The other challenge going forward is how the endotypes can be defined and incorporated into standard polysomnography reports to allow informed decision-making at the time of clinical assessment.

The complexity (read 'significant heterogeneity') of adult OSA patients means that utilizing one main 'success' measure such as AHI and applying physiological endotyping alone to try and predict surgical outcomes is a challenge. Device use outcomes may well be more predictable within such a framework. However, surgery is a detailed process that entangles an array of concepts into decision-making: patient/partner history, static anatomy (soft and hard tissue), weight and BMI, dynamic anatomy (awake/sleep endoscopy), risks/benefit profile and patient/partner preferences. The search to enhance pre-operative surgical predictability continues and will likely involve the best marriage of anatomy, physiology and realistic expectations.

KEYWORDS
endotyping, sleep apnoea, sleep disorder

CONFLICT OF INTEREST
None declared.

ORCID
Stuart G. MacKay https://orcid.org/0000-0002-7378-3515

LINKED CONTENT
This publication is linked to a related article. To view this article, visit https://doi.org/10.1111/resp.14280.

Stuart G. MacKay FRACS[1,2]
Andrew Jones FRACP[3,4]

[1]*Ear Nose and Throat, Illawarra ENT Head and Neck Clinic, Wollongong, New South Wales, Australia*
[2]*Ear Nose and Throat Surgery, University of Wollongong Graduate School of Medicine, Wollongong, New South Wales, Australia*
[3]*Respiratory and Sleep Medicine, Illawarra Sleep Medicine Centre, Wollongong, New South Wales, Australia*
[4]*Respiratory and Sleep Medicine, University of Wollongong Graduate School of Medicine, Wollongong, New South Wales, Australia*

Correspondence
Stuart G. MacKay
Email: sgmackay@ozemail.com.au

REFERENCES

1. Wong A-M, Landry SA, Joosten SA, Thomson LDJ, Turton A, Stonehouse J, et al. Examining the impact of multilevel upper airway surgery on the obstructive sleep apnoea endotypes and their utility in predicting surgical outcomes. Respirology. 2022. https://doi.org/10.1111/resp.14280
2. Eckert DJ. Phenotypic approaches to obstructive sleep apnoea – new pathways for targeted therapy. Sleep Med Rev. 2018;37:45–59. https://doi.org/10.1016/j.smrv.2016.12.003
3. Green KK, Kent DT, D'Agostino MA, Hoff PT, Lin H-S, Soose RJ, et al. Drug-induced sleep endoscopy and surgical outcomes: a multicenter cohort study. Laryngoscope. 2019 Mar;129(3):761–70.
4. Soares D, Sinawe H, Folbe AJ, Yoo G, Badr S, Rowley JA, et al. Lateral oropharyngeal wall and supraglottic airway collapse associated with failure in sleep apnea surgery. Laryngoscope. 2012;122(2):473–9.
5. Smith MM, Peterson E, Yaremchuk KL. The role of tonsillectomy in adults with tonsillar hypertrophy and obstructive sleep apnea. Otolaryngol Head Neck Surg. 2017;157(2):331–5.
6. Choi JH, Cho SH, Kim S-N. Predicting outcomes after uvulopalatopharyngoplasty for adult obstructive sleep apnea: a meta-analysis. Otolaryngol Head Neck Surg. 2016;155:904–13. https://doi.org/10.1177/0194599816661481
7. Puccia R, Woodson BT. Palatopharyngoplasty and palatal anatomy and phenotypes for treatment of sleep apnea in the twenty-first century. Otolaryngol Clin North Am. 2020;53(3):421–9. https://doi.org/10.1016/j.otc.2020.02.005
8. MacKay S, Lewis R, McEvoy D, Jooste S, Holt N. Surgical management of obstructive sleep apnoea: a position statement of the Australasian Sleep Association. Respirology. 2020;25:1292–308.
9. Lee CH, Shin H-W, Han DH, Mo J-H, Yoon I-Y, Chung S, et al. The implication of sleep position in the evaluation of surgical outcomes in obstructive sleep apnea. Otolaryngol Head Neck Surg. 2009;140(4):531–5. https://doi.org/10.1016/j.otohns.2008.12.023
10. Certal V, Nishino N, Camacho M, Capasso R. Reviewing the systematic reviews in OSA surgery. Otolaryngol Head Neck Surg. 2013;149:817–29. https://doi.org/10.1177/0194599813509959
11. Stuart MacKay A, Carney S, Catcheside PG, Chai-Coetzer CL, Chia M, Cistulli P. Effect of multilevel upper airway surgery vs medical management on the apnea-hypopnea index and patient-reported daytime sleepiness among patients with moderate or severe obstructive sleep apnea: the SAMS randomized clinical trial. JAMA. 2020;324(12):1168–79. https://doi.org/10.1001/jama.2020.14265

How to cite this article: MacKay SG, Jones A. Endotyping in sleep surgery: Not ready for primetime. Respirology. 2022. https://doi.org/10.1111/resp.14332