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Approach for Streamlining Measurement of Complex Physiological Phenotypes of Upper Airway Collapsibility

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Abstract

The critical closing pressure (P_{CRIT}), a quantitative assessment of upper airway collapsibility, is derived from pressure flow relationship during sleep. The analytic generation of the pressure flow relationships are non-standardized due to various regression models (linear, spline, median), breath characteristics (flow limited, non-flow limited) or known covariates (sleep stage, body position). We propose a GUI based P_{CRIT} Analysis Software (PAS) to streamline P_{CRIT} analysis and validate its reliability and accuracy compared to current analysis procedures.

Methods—Seventeen subjects underwent a physiology sleep study in which the P_{CRIT} was determined during NREM sleep. Data analysis was performed independently using three paradigms: 1) PAS (Igor Pro; median regression), 2) non-graphic statistics application (SAS; spline regression), and 3) manual spreadsheet calculations (Excel; linear regression). The reliability and accuracy of the PAS was examined through the agreement between each approach using Bland-Altman plots of the mean difference and within-individual variation using intra-class correlation (ICC).

Results—There was no difference in the group mean values for P_{CRIT} using the PAS (-1.7 ± 0.7 cm H₂O) compared to spline regression (-1.6 ± 0.7 cm H₂O; $p=0.69$) or linear regression (-2.1 ± 0.7 cm H₂O; $p=0.92$). The Bland-Altman analysis did not demonstrate a systematic bias between the

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PAS and either approach. There was a mean difference of 0.39 ± 0.2 cm H₂O between the PAS and linear regression approaches, with upper and lower limits of agreement of 1.81 and -1.02 cm H₂O, respectively. The PAS and spline analysis demonstrated an even smaller mean difference of -0.10 ± 0.1 cm H₂O, with upper and lower limits of 0.90 and -1.08 cm H₂O, respectively.

Conclusion—PAS preserves the reliability and accuracy of the original P_{CRIT} analysis methods while vastly improving their efficiency through graphic user interface and automation of analytic processes. Providing a standardized platform for physiologic data processing offers the ability to implement quality assurance and control procedures for multicenter studies as well as cost saving by improving the efficiency of complex repetitive tasks.

INTRODUCTION

Obstructive sleep apnea (OSA) is a condition where the airway collapses partially or completely during sleep and results in limited breathing^{1,2}. Upper airway collapsibility is commonly measured by the critical pressure, P_{CRIT}, which is the pressure at which flow ceases³⁻⁸. P_{CRIT} is a useful index of disease severity since patients exhibiting OSA have higher P_{CRIT} values than normal patients⁹⁻¹⁶.

While there are currently efficient methods in place for collecting sleep data, the analytic generation of the pressure flow relationships remains a time-consuming and cumbersome task¹⁷⁻²⁰. Procedures are non-standardized due to varying regression models (linear, spline, median), breath characteristics (flow limited, non-flow limited) or known covariates (sleep stage, body position). In general, trained researchers and technicians are expected to mark events in the sleep recording, extract the data into text files and spreadsheets, sort through many rows and columns of data, extensively review individual numbers, switch software platforms to perform statistical analysis of P_{CRIT} and separately graph the data to visually display a pressure-flow relationship. The process is seldom linear, whereby researchers often need to repeat analytic steps. Needless to say, there are considerable time commitments in these steps. Inefficiencies in the data analysis process limit the applicability of *physiological measurements* in epidemiology and genetic cohorts, thus there is need to streamline methods.

The data processing steps of physiological measurement can be reasonably repetitive, therefore an on-time solution is possible for streamlining data export, graphically displaying the extracted physiological values, categorizing experimental conditions and integrating relevant calculations and statistics. This makes immediate review of the data possible, allowing effortless error detection and correction while creating an organized structure for database entry. The data analysis software, in a numerical computing environment with 4th generation programming language, was chosen for its built-in commands that facilitate generating graphical displays of large data sets. In the current paper, we describe the components of a streamlined P_{CRIT} analysis system and its application to investigating upper airway properties. More specifically, we examine the agreement between standard analytic approaches with the novel P_{CRIT} analysis system. Improving efficiencies in physiological measurements will enhance the applicability of their integration in large clinical and community cohorts.

CONCEPTUAL APPROACH: Upper Airway Collapsibility (P_{CRIT})

Starling Resistor Model

In the Starling resistor model, the upper airway is represented as a simple tube with a collapsible segment bounded by two more rigid segments upstream (nasal segment) and downstream (hypopharyngeal segment). The segments upstream and downstream to the

collapsible site have fixed diameters and resistances across all upstream and downstream pressures. There are several features important to the use of inspired airflow to estimate upper airway collapsibility²¹. It has been shown that flow cannot occur until the pressure upstream from the collapsible segment exceeds the upper airway collapsing pressure (P_{CRIT})²²⁻²⁸. Once flow is established, a fall in pressure due to frictional and/or convective losses occurs across the collapsible segment sufficient to maintain a near constant pressure at the locus of collapse that equals a critical surrounding pressure (P_{CRIT}). The Starling resistor model is a mechanical analog of the upper airway which assumes an infinitely collapsible segment and the absence of neural activity in the structure.

Upper Airway Airflow during Airflow Limitation

Under the conditions of airflow limitation, maximal flow (V_{Imax}) is determined by the gradient between the upstream nasal pressure (P_{N}) and the P_{CRIT} , and the resistance (R_{N}) upstream as described in the equation.

$$V_{\text{Imax}} = (P_{\text{N}} - P_{\text{CRIT}}) \div R_{\text{N}} \quad \text{Equation 1}$$

Flow is independent of the changes downstream (hypopharyngeal pressure)^{22,29-31}. Under flow-limited conditions, pressure downstream to the site of collapse no longer influences maximal inspiratory airflow (V_{Imax}). Rather, V_{Imax} varies solely with changes in the upstream nasal pressure²¹ and increases proportionately with elevations in nasal pressure, allowing us to determine P_{CRIT} assuming a constant sloped pressure-flow relationship.

Since V_{Imax} during inspiratory airflow limitation is determined solely by upper airway characteristics rather than the level of ventilatory drive, any increase in the level of mean inspiratory airflow would be attributed to increases in upper airway neuromuscular responses or upper airway biochemical and physical properties. Similarly, during the inspiratory airflow limited condition a change in airflow can be used as a marker for responses in upper airway properties to a given stimulus.

The P_{CRIT} of the upper airway can be extrapolated by plotting the maximal inspiratory airflow (V_{Imax}) against P_{N} during sleep-induced flow-limited inspiration^{27,32}. Such flow limitation is determined by the presence of a flattened flow vs. time contour³³⁻³⁶. The flow-limited segment of the V_{Imax} vs. P_{N} relationship can be identified using a median segmented regression approach between the upper and lower inflection points of the sloped (flow-limited) segment (see Figure 1).

METHODS

Subjects

A total of 17 subjects participated in the current study. Seven of the patients were non-apneic (4 male, 3 female) and ten were previously diagnosed with sleep apnea (7 male, 3 female). Sleep apnea was defined as a respiratory disturbance index (RDI) greater than 10 events per hour (Table 1). Written informed consent was obtained from each participant for this study, which was approved by the Johns Hopkins Medical Institution Human Investigational Review Board.

Procedures

Polysomnographic Data Acquisition Process—Polysomnograms were generated using full montage acquisition system (Embla N7000, Somnologica, Medcare, Buffalo, NY), and included signals: left and right electrooculograms (EOG), electroencephalogram (EEG), submental electromyogram (EMG), electrocardiogram (EKG), oxyhemoglobin saturation

(SpO₂), transcutaneous CO₂ level (TcCO₂), inductance plethysmography, airflow via a pneumotachograph and oronasal thermistor, and body position. Participants wore nasal continuous positive airway pressure (CPAP) masks, while a pneumotachograph (Hans Rudolph model #4830, Hans Rudolph, Kansas City, MO) and pneumotachograph amplifier (Hans Rudolph model #1, Series 1110) measured airflow. Nasal pressure (P_N) was adjusted to induce airway collapse using a modified CPAP device (ResMed Ltd, Bella Vista, NSW, Australia) capable of generating pressure drops from -20 to 20 cm H₂O.

Upper Airway Collapsibility (P_{CRIT}) measurement—In order to perform P_{CRIT} analysis, P_N is initially held at a level sufficient to prevent airflow limitation. Intermittently P_N is reduced in subsequent pressure drops until a level where there is no flow. Flow measurements are extracted from several breaths at each P_N level (pressure drop) for later analysis. A 'series' denotes the collection of pressure-flow values from multiple P_N pressure drops used to determine P_{CRIT}.

Hardware and Software Requirements—The routines described can be performed using a technical graphing and data analysis software package for Macintosh and Windows (Igor Pro software, version 6.12a, Wavemetrics Inc., <http://www.wavemetrics.com>). The procedure was developed on a ViewSonic VX2739wm monitor and an Intel Core 2 Duo E8400 PC with 3.00 GHz processors and 3.25 GB of RAM, using Microsoft Windows XP Professional Version 2002, Service Pack 2. Minor adjustments may be needed to adapt the program to run on the Macintosh operating system. Default parameters such as the path to executable files are also required to be established during setup. It is also possible to incorporate workflow features such as database integration and server side run time analysis procedures to complement this program.

Respiratory Airflow Data Recording and Breath Detection Algorithm—The data was analyzed using Somnologica Studio or RemLogic acquisition and review software (Embla, Buffalo, NY)(Figure 2). Custom plug-in software developed using the Somnologica SDK 3.2 (Emsotec GmbH, Germany) provides a combination of semi-automated peak detection and cyclic waveform algorithms used to extract breath-by-breath values from respiratory signals. In brief, analysis is targeted to select periods of the airflow trace (or the complete trace if required): first, to mark the inspiratory phase of the respiratory cycle; second, to detect the peak inspiratory airflow; and third, to export the breath parameters. An example of the output from the breath-by-breath data is displayed in Table 2, which is saved in spreadsheet file format (.xls). Saving the data into a database format is an alternate method for archiving individual breath-by-breath variables.

Upper Airway Collapsibility Data Analysis using P_{CRIT} Analysis Software (PAS)—The main approach employed to import data into the PAS is to directly load breath-by-breath data from a spreadsheet file as shown in Table 2. A file selector panel acts as the primary data explorer to provide a flexible directory search option. Users may select an experimental data folder, which serves as a primary root folder, in order to search for files of known type and specify the depth of folders to inspect within the primary root folder. It is possible to narrow file search criteria by limiting returned file extensions (e.g. .ewp, .xls, .txt). From the file selector panel, the chosen file can be either loaded into the PAS or opened in its native application (e.g. Somnologica or RemLogic if viewing .ewp files). Alternatively, a completely flexible browse option allows files to be manually imported into the PAS. Data for direct import into PAS must follow the given format in Table 2. The PAS is constrained to a maximum of 60 pressure drops and 8 series of pressure drops.

Prior to importing data into the PAS, radio button and variable settings may be selected or modified from a settings panel to optimize the analysis process. These options provide the software with information on criteria to group breaths, calculate $V_{I\max}$, implement necessary unit conversions, and/or perform breath-by-breath calculations. Once the data is imported, PAS creates an overview plot, a pressure-airflow plot and a data selection panel. The overview plot displays the number of series, pressure drops and breaths per drop, P_N , sleep position, and sleep stage for each breath. Combined, these data allow a user to obtain a snapshot of the breath-by-breath data extracted from the raw pressure and airflow traces, with respect to the standard sleep studies analysis from Remlogic. The overview plot also serves as a graphical reference point data analysis of upper airway collapsibility in the PAS. The pressure-airflow plot depicts the relationship between maximal inspiratory flow ($V_{I\max}$) and P_N . In the PAS, the pressure-airflow plot is a dynamic display and focus for data output: it presents grouping of breaths at set pressure levels (bins) for generating pressure-airflow median regression analysis, the medians of each pressure bin, and the slopes between medians. Each point on the pressure-airflow plot corresponds to one on the overview plot, allowing informational display as well as deletion, alteration, or restoration of selected data points from either plot. Users may customize pressure assignments and threshold median slope values on a bin-by-bin basis to determine which data points are incorporated in the median regression. Further customization is possible through a *data selection panel*, which allows users to determine the breaths (data points) included in the pressure-airflow plot. This panel can limit analysis to a particular series, sleep stage, or body position as well as exclude pressure drops coinciding with anomalous events. The collection of data display, review and interactive windows provide the tools for easy data revision and finalization.

Users may wish to compare pressure-airflow plots under various experimental conditions or between individuals. The state of pressure-airflow plots can be copied and preserved, thus allowing simultaneous review of multiple data sets (Figure 3), such that comparisons within and between P_{CRIT} studies are straightforward. PAS menus provide a list of commonly used tables for easy data display, and shortcuts allow keystroke-interfacing with the program: to open, close, refresh windows, save, load files, and reset the program.

Analysis

To determine the utility of the streamlined approach for determining upper airway collapsibility using the PAS, we used three separate approaches to generate passive pressure-flow curves for each upper airway physiology study. The approaches were performed in random order and independent of one another. The analytical paradigms employed were 1) standard linear regression using Excel 2010 (Microsoft, Redmond, Washington), 2) segmented regression (spline) analysis using SAS 9.3.1 (Cary, North Carolina) and 3) median regression using the PAS (Custom Procedure for Igor Pro as described above).

We examined the validity of the P_{CRIT} values determined using the PAS by comparing it to each of the other analytical approaches^{27,37}. First, differences between P_{CRIT} values were assessed using student paired t-tests. Second, the intraclass-correlation (ICC) between measurements, an assessment of the within-individual variation, was determined using the method described by Deyo et al³⁸. An ICC of 1.0 would indicate an absence of within-individual variability between analytic approaches. Third, Bland-Altman plots of the difference in approaches vs. the average of the separate values were examined for evidence of systematic bias, the presence of heteroscedasticity, and to identify the limits of agreement that bound the mean difference between the P_{CRIT} values. Statistical significance was defined as $p < 0.05$ and data are presented as mean $\pm$ SEM unless otherwise stated.

RESULTS

Demographic, anthropometric, polysomnographic characteristics for all 17 subjects are displayed in Table 1. The average P_{CRIT} for these subjects, as determined by the PAS, was -1.7 ± 0.7 cm H₂O. In comparison, the average was -2.1 ± 0.7 cm H₂O and -1.6 ± 0.7 cm H₂O when using linear regression and spline analysis respectively. Paired t-tests demonstrated a non-significant difference between the PAS and both linear regression ($p=0.69$) and spline analysis ($p=0.92$). The ICC was 0.95 for comparison with linear regression and 0.99 for spline analysis, indicating extremely good consistency between these approaches. The Bland-Altman analysis did not demonstrate a systematic bias between either set of measurements (Figure 4A-B). There was a mean difference of 0.39 ± 0.2 cm H₂O between the PAS and linear regression approaches, with upper and lower limits of agreement of 1.81 and -1.02 cm H₂O, respectively. The PAS and spline analysis demonstrated an even smaller mean difference of -0.10 ± 0.1 cm H₂O, with upper and lower limits of 0.90 and -1.08 cm H₂O.

DISCUSSION

We have described a visual analysis system for processing complex physiological parameters in a streamlined approach. The findings in this study demonstrate that the software is both valid and reliable in streamlining P_{CRIT} measurements as there is no significant difference in the calculated values for upper airway collapsibility between the Igor-based P_{CRIT} analysis software, and the formerly established methods of linear regression and spline analysis.

While precision of the measurement is consistent throughout the three paradigms, the PAS provides a considerable boost in efficiency, by eliminating many redundant and time-consuming steps through the use of a graphic user interface and automation of analytic processes. These steps include the manual organization and sorting of physiological protocol steps, manipulation of large data spreadsheets to identify specific outlying values, and data point re-exportation and recovery, to name a few. The streamlined process also greatly promotes the user's ability to quickly perform subset analyses, providing the ability to view only certain subsets of the entire dataset such as displaying by stages of sleep, times of the night, or any particular breath type. While specific analysis time is largely dependent on the complexity of the study, we estimate that this software could decrease the time required to analyze any particular study by as much as 50%. In the current study we have shown that while maintaining the same accuracy and precision, streamlining analytic processes in physiological studies utilizing software solution can overcome time-consuming methods and ultimately facilitate efficient review. In addition to hastening the initial analysis period, the software approach described in the current study more readily allows for post-analysis modification and re-examination of values, if required by the user. This improved efficiency, accuracy, and reliability may translate into cost savings and reduce the amount of training investigators need to generate pressure flow relationships from sleep data. PAS provides a standardized platform for physiologic data processing, which offers the ability to implement quality assurance and control procedures for multicenter studies.

The main utility and benefits of using the PAS are to visually aid the analysis process to be able to implement an overview that assists quality control and expedites data review. Figure 3 Panel A visually captures the input data for the entire study and provide a display that allows the user to easily identify inconsistencies. The x-axis of the overview panel is equivalent to the row number in Table 2 of each breath identified in the raw data illustrated in Figure 2. The first of the four plots on the overview panel displays the number of breaths on the y-axis for each nasal pressure drop with a color spectrum that starts from the red end

used to segregate subsequent drops. Second from the top is the level of nasal pressure for each breath grouped using the color of a series of pressure drops. The color of each nasal pressure series of the overview panel corresponds to the series checkbox filters on the selector panel displayed in Figure 3 Panel C. The third and fourth traces are the body position and the sleep stage hypnogram, respectively. Figure 3 Panel B displays the nasal pressure (x-axis) versus the V_{max} (y-axis) for each breath in the series selected from the selector panel C. Immediately above the pressure-flow plot are indicator bars that signify a pressure level bin of data for inclusion in the median regression analysis. This visual display of the data allows a technician or investigator to easily identify and correct errant values, thus expediting the analytic process.

PAS would specifically be beneficial to clinical investigations of sleep apnea. Sleep apnea is due to physiologic disturbances in upper airway mechanics and neural control. Mechanical loads on the upper airway can be quantified by measuring the P_{CRIT} under conditions of relative neuromuscular hypotonia (passive P_{CRIT}).⁴²⁻⁴⁴ Neural activation can be determined by measuring P_{CRIT} responses to prolonged periods of airflow obstruction, which recruit the upper airway musculature (active P_{CRIT}). Differences between active and passive P_{CRIT} represent an individual's neural compensatory capacity, which has been shown to be markedly reduced in sleep apnea patients compared to age, weight and sex matched normal individuals.^{1,45} Thus, sleep apnea susceptibility is defined by these specific quantifiable physiologic metrics. Although methods for measuring critical pressure have been well-established in physiologic research, there are extensive methodological and analytic requirements which limit their broad applicability in clinical research.

Improving the analytic efficiencies will allow these important pathophysiological measurements to be incorporated on a larger scale across multiple sites of investigation. Furthermore, there are multiple and various physiologic and polysomnographic recording software that are employed to capture raw data from sleep and breathing waveforms, as such a standard analytic tool across platforms would extend the flexibility of performing these measurements. Integration of a quantitative airflow measurement in large community or clinical cohorts that are simultaneously characterized for activities of daily living and clinical co-morbidities would now provide an opportunity to demonstrate the association of streamlined physiological measurements with underlining respiratory pathology. The deployment of the streamlined quantitative phenotypic characterization in those with chronic pulmonary disease, obstructive sleep apnea, and in children pre- and -post upper airway surgery is important determining change in disease severity over time and to determine the natural history of upper airway collapsibility.

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Reference List

- (1). Sullivan CE, Issa FG. Pathophysiological mechanisms in obstructive sleep apnea. *Sleep*. 1980; 3(3-4):235–246. [PubMed: 7221334]
- (2). Schwartz AR, O'Donnell CP, Baron J, et al. The hypotonic upper airway in obstructive sleep apnea: role of structures and neuromuscular activity. *Am J Respir Crit Care Med*. 1998; 157(4 Pt 1):1051–1057. [PubMed: 9563718]

- (3). Schwartz AR, Smith PL, Wise RA, Gold AR, Permutt S. Induction of upper airway occlusion in sleeping individuals with subatmospheric nasal pressure. *J Appl Physiol.* 1988; 64(2):535–542. [PubMed: 3372411]
- (4). Smith PL, Wise RA, Gold AR, Schwartz AR, Permutt S. Upper airway pressure-flow relationships in obstructive sleep apnea. *J Appl Physiol.* 1988; 64(2):789–795. [PubMed: 3372436]
- (5). Schwartz AR, Smith PL, Wise RA, Bankman I, Permutt S. Effect of positive nasal pressure on upper airway pressure-flow relationships. *J Appl Physiol.* 1989; 66(4):1626–1634. [PubMed: 2659574]
- (6). Smith PL, Schwartz AR, Gauda E, Wise R, Brower R, Permutt S. The modulation of upper airway critical pressures during sleep. *Prog Clin Biol Res.* 1990; 345:253–258. [PubMed: 2377636]
- (7). Gleadhill IC, Schwartz AR, Schubert N, Wise RA, Permutt S, Smith PL. Upper airway collapsibility in snorers and in patients with obstructive hypopnea and apnea. *Am Rev Respir Dis.* 1991; 143(6):1300–1303. [PubMed: 2048817]
- (8). Schwartz AR, O'Donnell CP, Baron J, et al. The hypotonic upper airway in obstructive sleep apnea: role of structures and neuromuscular activity. *Am J Respir Crit Care Med.* 1998; 157(4 Pt 1):1051–1057. [PubMed: 9563718]
- (9). Schwartz AR, Gold AR, Schubert N, et al. Effect of weight loss on upper airway collapsibility in obstructive sleep apnea. *Am Rev Respir Dis.* 1991; 144(3 Pt 1):494–498. [PubMed: 1892285]
- (10). Schwartz AR, Schubert N, Rothman W, et al. Effect of uvulopalatopharyngoplasty on upper airway collapsibility in obstructive sleep apnea. *Am Rev Respir Dis.* 1992; 145(3):527–532. [PubMed: 1546831]
- (11). Schwartz AR, Eisele DW, Smith PL. Pharyngeal airway obstruction in obstructive sleep apnea: pathophysiology and clinical implications. *Otolaryngol Clin North Am.* 1998; 31(6):911–918. [PubMed: 9838008]
- (12). Patil SP, Schneider H, Schwartz AR, Smith PL. Adult obstructive sleep apnea: pathophysiology and diagnosis. *Chest.* 2007; 132(1):325–337. [PubMed: 17625094]
- (13). Kirkness JP, Schwartz AR, Schneider H, et al. Contribution of male sex, age, and obesity to mechanical instability of the upper airway during sleep. *J Appl Physiol.* 2008; 104(6):1618–1624. [PubMed: 18420722]
- (14). Gold AR, Smith PL, Schwartz AR. The study of maximal nasal inspiratory flow in humans. *J Appl Physiol.* 1996; 81(2):627–635. [PubMed: 8872627]
- (15). Gleadhill IC, Schwartz AR, Schubert N, Wise RA, Permutt S, Smith PL. Upper airway collapsibility in snorers and in patients with obstructive hypopnea and apnea. *Am Rev Respir Dis.* 1991; 143(6):1300–1303. [PubMed: 2048817]
- (16). Boudewyns A, Schwartz AR, Van de Heyning PH. Upper airway collapsibility: measurement techniques and therapeutic implications. *Acta Otorhinolaryngol Belg.* 2002; 56(2):121–125. [PubMed: 12092320]
- (17). Patil SP, Punjabi NM, Schneider H, O'Donnell CP, Smith PL, Schwartz AR. A simplified method for measuring critical pressures during sleep in the clinical setting. *Am J Respir Crit Care Med.* 2004; 170(1):86–93. [PubMed: 15070819]
- (18). Kirkness JP, Peterson LA, Squier SB, et al. Performance characteristics of upper airway critical collapsing pressure measurements during sleep. *Sleep.* 2011; 34(4):459–467. [PubMed: 21461324]
- (19). Boudewyns A, Punjabi N, Van de Heyning PH, et al. Abbreviated method for assessing upper airway function in obstructive sleep apnea. *Chest.* 2000; 118(4):1031–1041. [PubMed: 11035674]
- (20). McGinley BM, Schwartz AR, Schneider H, Kirkness JP, Smith PL, Patil SP. Upper airway neuromuscular compensation during sleep is defective in obstructive sleep apnea. *J Appl Physiol.* 2008; 105(1):197–205. [PubMed: 18403451]
- (21). Gold AR, Schwartz AR. The pharyngeal critical pressure. The whys and hows of using nasal continuous positive airway pressure diagnostically. *Chest.* 1996; 110(4):1077–1088. [PubMed: 8874271]

- (22). Smith PL, Wise RA, Gold AR, Schwartz AR, Permutt S. Upper airway pressure-flow relationships in obstructive sleep apnea. *J Appl Physiol.* 1988; 64(2):789–795. [PubMed: 3372436]
- (23). Gleadhill IC, Schwartz AR, Schubert N, Wise RA, Permutt S, Smith PL. Upper airway collapsibility in snorers and in patients with obstructive hypopnea and apnea. *Am Rev Respir Dis.* 1991; 143(6):1300–1303. [PubMed: 2048817]
- (24). Schwartz AR, Eisele DW, Hari A, Testerman R, Erickson D, Smith PL. Electrical stimulation of the lingual musculature in obstructive sleep apnea. *J Appl Physiol.* 1996; 81(2):643–652. [PubMed: 8872629]
- (25). Schwartz AR, O'Donnell CP, Baron J, et al. The hypotonic upper airway in obstructive sleep apnea: role of structures and neuromuscular activity. *Am J Respir Crit Care Med.* 1998; 157(4 Pt 1):1051–1057. [PubMed: 9563718]
- (26). Sforza E, Petiau C, Weiss T, Thibault A, Krieger J. Pharyngeal Critical Pressure in Patients with Obstructive Sleep Apnea Syndrome. Clinical implications. *Am J Respir Crit Care Med.* 1999; 159(1):149–157. [PubMed: 9872833]
- (27). Patil SP, Punjabi NM, Schneider H, O'Donnell CP, Smith PL, Schwartz AR. A simplified method for measuring critical pressures during sleep in the clinical setting. *Am J Respir Crit Care Med.* 2004; 170(1):86–93. [PubMed: 15070819]
- (28). Gold AR, Marcus CL, Dipalo F, Gold MS. Upper airway collapsibility during sleep in upper airway resistance syndrome. *Chest.* 2002; 121(5):1531–1540. [PubMed: 12006440]
- (29). Schwartz AR, Schubert N, Rothman W, et al. Effect of uvulopalatopharyngoplasty on upper airway collapsibility in obstructive sleep apnea. *Am Rev Respir Dis.* 1992; 145(3):527–532. [PubMed: 1546831]
- (30). Schwartz AR, Gold AR, Schubert N, et al. Effect of weight loss on upper airway collapsibility in obstructive sleep apnea. *Am Rev Respir Dis.* 1991; 144(3 Pt 1):494–498. [PubMed: 1892285]
- (31). Schneider H, O'hearn DJ, Leblanc K, et al. High-flow transtracheal insufflation treats obstructive sleep apnea. A pilot study. *Am J Respir Crit Care Med.* 2000; 161(6):1869–1876. [PubMed: 10852759]
- (32). Boudewyns A, Punjabi N, Van de Heyning PH, et al. Abbreviated Method for Assessing Upper Airway Function in Obstructive Sleep Apnea. *Chest.* 2000; 118(4):1031–1041. [PubMed: 11035674]
- (33). Farre R. Inspiratory flow limitation in obstructive sleep apnoea patients. *Clin Sci (Lond).* 2004; 106(6):563–565. [PubMed: 14738414]
- (34). Hudgel DW, Hendricks C, Hamilton HB. Characteristics of the upper airway pressure-flow relationship during sleep. *J Appl Physiol.* 1988; 64(5):1930–1935. [PubMed: 3391893]
- (35). Mansour KF, Rowley JA, Meshenish AA, Shkoukani MA, Badr MS. A mathematical model to detect inspiratory flow limitation during sleep. *J Appl Physiol.* 2002; 93(3):1084–1092. [PubMed: 12183506]
- (36). Morgenstern C, Schwaibold M, Randerath WJ, Bolz A, Jane R. Assessment of changes in upper airway obstruction by automatic identification of inspiratory flow limitation during sleep. *IEEE Trans Biomed Eng.* 2009; 56(8):2006–2015. [PubMed: 19457737]
- (37). Patil SP, Schneider H, Marx JJ, Gladmon E, Schwartz AR, Smith PL. Neuromechanical control of upper airway patency during sleep. *J Appl Physiol.* 2007; 102(2):547–556. [PubMed: 17008440]
- (38). Deyo RA, Diehr P, Patrick DL. Reproducibility and responsiveness of health status measures. Statistics and strategies for evaluation. *Control Clin Trials.* 1991; 12(4 Suppl):142S–158S. [PubMed: 1663851]

Figure 1.

Custom analysis and export functions integrated into standard PSG software for determining upper airway properties from an overnight sleep recording where the nasal pressure (P_N) is intermittently reduced to examine the airflow (V) responses. Periods of the recording are selected to perform breath-by-breath analysis that marks inspiration from each breath and extracts the peak inspiratory airflow.

Figure 2.

An illustrative representation of maximal inspiratory airflow ($V_{I\max}$) versus nasal pressure showing distinct regions of the pressure-flow curve as described using the Starling resistor model: a completely occluded segment (section I), a flow-limited (section II), and a non-flow-limited segment (section III). The segment containing flow-limited breaths is bounded by the critical collapsing pressure (P_{CRIT}) and by the effective therapeutic CPAP pressure (P_{CPAP}). Regression analysis of the flow-limited section of the pressure-flow plot is used to establish the P_{CRIT} as the nasal pressure at which airflow approaches zero. (modified from ²⁷)

Figure 3.

An illustration of completed P_{CRIT} analysis for one series of pressure and airflow data points (blue circles). The multicolored horizontal bars indicate the individual range of pressure levels used to perform median regression for the entire pressure-flow data series. The summary statistics for the regression equation (in the form $V_{\max} = xP_N + \text{constant}$) are provided on the right of the graph which includes: P_{CRIT} where $V_{\max} = 0$; $R_{\text{US}} = 1/\text{slope}$; and P & V_I low and high values indicating the range over which the analysis is performed.

Figure 4.

Bland-Altman plots displaying the difference between analysis methods of P_{CRIT} (using either the median regression [PAS] vs simple linear regression [Excel; panel A] or spline analysis [SAS; panel B] and plotted against the average of the measurements. The mean difference (solid line) is not different from zero (dashed) and the limits of agreement (dotted lines) are represented as ± 2 standard deviations.

TABLE 1

Variable	Subjects (n=17)
Anthropometry	
Age (yr)	58.1 $\pm$ 2.3
Sex	11 M/6 F
Height (cm)	174.0 $\pm$ 1.7
Weight (kg)	88.7 $\pm$ 4.4
BMI(kg/m ²)	29.7 $\pm$ 1.4
Polysomnography	
TST (min)	353.3 $\pm$ 17.5
Sleep Efficiency (%TST)	80.7 $\pm$ 3.3
NREM (%TST)	84.6 $\pm$ 1.5
Stage 1	26.6 $\pm$ 5.5
Stage 2	50.1 $\pm$ 4.2
Stage 3	7.2 $\pm$ 2.5
REM (%TST)	16.1 $\pm$ 1.6
Total AHI (events/h)	32.1 $\pm$ 8.9
NREM AHI (events/h)	31.6 $\pm$ 8.9
REM AHI (events/h)	32.7 $\pm$ 10.3
Hypopnea Percentage	
NREM	77.5 $\pm$ 6.6
REM	62.1 $\pm$ 8.3
Arterial SaO ₂ (%)	
Average baseline value	94.1 $\pm$ 0.6
Average low value	89.7 $\pm$ 0.6

TABLE 2

BREATH-BY-BREATH VARIABLE OUTPUT

StartTime	StopTime	StartSample	StopSample	T_insp	T_tot	Vmean	Vmax	Pn_Vimax_	Vstart	Vstop	Sleep	Position	Period
3:48:23 AM	3:48:25 AM	2796123	2796343	2.20	3.92	12.28	7.43	-0.91	29.63	29.74	S2	Supine	Passive Drop
3:48:27 AM	3:48:29 AM	2796515	2796720	2.05	4.24	10.48	4.53	-0.84	33.92	33.45	S2	Supine	Passive Drop
3:48:31 AM	3:48:33 AM	2796939	2797092	1.53	4.44	11.90	5.19	-1.03	35.04	34.94	S2	Supine	Passive Drop
3:48:35 AM	3:48:37 AM	2797383	2797557	1.74	3.88	11.78	5.26	-0.91	35.23	35.91	S2	Supine	Passive Drop
3:48:39 AM	3:48:41 AM	2797771	2797956	1.85	4.05	10.86	4.27	-0.88	32.34	32.62	S2	Supine	Passive Drop
3:48:43 AM	3:48:45 AM	2798176	2798349	1.73	4.01	12.52	5.45	-0.88	31.87	31.83	S2	Supine	Passive Drop
3:48:47 AM	3:48:49 AM	2798577	2798773	1.96	4.15	13.95	5.32	-0.83	34.71	34.60	S2	Supine	Passive Drop
3:48:52 AM	3:48:53 AM	2798992	2799187	1.95	4.13	12.30	3.94	-0.84	30.29	30.25	S2	Supine	Passive Drop
3:48:56 AM	3:48:57 AM	2799405	2799587	1.82		13.95	6.44	-0.86	35.17	35.35	S2	Supine	Passive Drop
3:52:34 AM	3:52:36 AM	2821286	2821454	1.68	4.49	32.24	25.61	-2.90	58.95	59.15	S2	Supine	Passive Drop
3:52:39 AM	3:52:41 AM	2821735	2821936	2.01	4.48	36.97	31.48	-2.91	57.50	57.63	S2	Supine	Passive Drop
3:52:43 AM	3:52:45 AM	2822183	2822389	2.06	4.26	37.03	28.51	-2.88	59.88	60.11	S2	Supine	Passive Drop
3:52:48 AM	3:52:49 AM	2822609	2822778	1.69	3.92	33.78	24.96	-2.90	57.64	58.08	S2	Supine	Passive Drop
3:52:52 AM	3:52:53 AM	2823001	2823169	1.68	4.12	32.94	25.61	-2.86	61.13	61.31	S2	Supine	Passive Drop
3:52:56 AM	3:52:57 AM	2823413	2823560	1.47	4.03	35.03	27.52	-2.88	59.74	59.99	S2	Supine	Passive Drop
3:53:00 AM	3:53:02 AM	2823816	2824006	1.90	4.85	33.94	27.06	-2.90	58.62	58.42	S2	Supine	Passive Drop
3:53:05 AM	3:53:06 AM	2824301	2824483	1.82	4.39	35.35	30.16	-2.86	55.51	55.46	S2	Supine	Passive Drop
3:53:09 AM	3:53:11 AM	2824740	2824939	1.99		35.73	31.81	-2.88	58.28	58.19	S2	Supine	Passive Drop

For each breath-by-breath parameter (variable name; format or units) the inspiration start and stop times (StartTime, StopTime; time), start and stop sample number in milliseconds from the beginning of the recording (StartSample, StopSample; number), inspiratory time (T_insp; s), total respiratory duration* (T_tot; s), mean inspiratory airflow (Vmean, L/min or L/s), peak inspiratory airflow (Vimax; L/min or L/s), nasal mask pressure (Pn_Vimax_; cm H₂O), the airflow value at inspiration start and stop times (Vstart, Vstop; L/min or L/s), sleep stage (Sleep; text), body position (Position; text), experimental condition/period indicator (Period; text). *Note that respiratory duration is calculated as the time between start inspiration of a breath and the following breath. In the case where there is no breath immediately following, T_tot is not calculated.