Research Article

Positive airway pressure therapy adherence and outcomes in obstructive sleep apnea: An exploratory longitudinal retrospective randomized chart review

Daniel Stevens[1][a], Michaela Title[1], Kathleen Spurr[2], Debra Morrison[3]

[1] School of Health and Human Performance, Dalhousie University, [2] School of Health Sciences, Dalhousie University, [3] Faculty of Medicine, Dalhousie University

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Abstract

Background

Positive airway pressure (PAP) therapy is prescribed to patients with obstructive sleep apnea (OSA). A commonly used definition for PAP therapy adherence is based upon the minimum requirements to receive Medicare coverage in the US, defined as PAP usage of four or more hours per night on 70 percent of nights for at least 30 consecutive days. However, little evidence exists to support this definition for PAP therapy adherence. Therefore, the present study sought to determine the efficacy of the present definition of PAP therapy adherence on longitudinal outcomes in patients with OSA, using objectively measured PAP device usage time.

Methods

An exploratory longitudinal, retrospective, randomized chart review was done to assess clinical outcomes between patients with OSA who were defined as PAP therapy adherent (n=50) and non-adherent (n=50) during an eight-year observation period.

Results

No significant differences were shown between groups for mortality, hospitalizations, or development of co-morbidities during the observation period. However, logistic regression showed significantly higher odds of adherence in male patients compared to female patients (OR=8.519; 95%CI=1.301–55.756; p=0.025) and significantly lower odds of adherence in patients with higher normal (OR=0.039; 95%CI=0.005–0.392; p=0.003), mild excessive (OR=0.039; 95%CI=0.003–0.517; p=0.014), and severe excessive (OR=0.088; 95%CI=0.012–0.635; p=0.016) daytime sleepiness compared to patients with lower normal daytime sleepiness. An increasing number of hospitalizations also corresponded with a significant decrease in odds of being adherent (OR=0.741; 95%CI=0.551–0.995; p=0.046).

Conclusion

The present study supports a steadily growing body of literature calling for more consideration and evidence to support a definition of PAP therapy adherence that is clinically meaningful.

a Corresponding author: Daniel Stevens, School of Health and Human Performance, Division of Kinesiology, Faculty of Health, Dalhousie University, Stairs House, 6230 South St., PO BOX 15000, Halifax NS, B3H 4R2, CANADA. . Email: d.stevens@dal.ca TEL: +1 (902) 494 6789 FAX: +1 (902) 494 5120

INTRODUCTION

Respiratory therapists play an integral role in the management of patients with sleep disordered breathing and are frequently involved in decisions related to the administration of positive airway pressure (PAP) therapy in patients with obstructive sleep apnea (OSA). PAP therapy delivers positively pressurized airflow to the upper airway via a variety of interfaces, including nasal, oronasal, or full-face mask. The pressure opens the airway, preventing the soft tissue from collapsing during sleep, which minimizes the periodic reduction or cessation of breathing during sleep and, consequently, the recurrent arousal from sleep and hypoxemia.[1,2] In patients with OSA, PAP therapy has been shown to significantly reduce daytime sleepiness and hypertension; improve quality of life measures[3,4]; and decrease morbidity and mortality in patients with co-existing heart failure, hypertension, and myocardial ischemia and infarction.[5,6]

Despite the widespread usage of PAP therapy in the clinical management of OSA, there are no established guidelines in the literature regarding the wear time duration of the device to discern meaningful patient benefits.[7] A commonly used definition for PAP adherence is based upon the minimum adherence requirements to receive Medicare coverage in the United States (US), defined as PAP usage of four or more hours per night on 70 percent of nights for at least 30 consecutive days.[8] However, clinical evidence is limited surrounding the validity of this cut-off point in OSA patients.[7] Observational studies have found a significant reduction in mortality with four or more hours per night of PAP therapy compared to no usage[9-12]; however, one study showed that when compared to PAP usage of less than four hours per night, no significant reduction in mortality was shown.[10] Randomized controlled trials (RCTs) have reported that PAP therapy adherence of four or more hours per night significantly reduced the risk of cardiovascular (CV) events compared to adherence of less than four hours per night.[13,14] However, some RCTs report a lack of association between PAP therapy and secondary CV disease prevention.[14-16] Due to stringent eligibility criteria, RCTs evaluating the impact of PAP therapy on CV outcomes were performed in minimally symptomatic patients with moderate-to-severe OSA, which precludes the generalization of their findings to more representative clinical populations with OSA.[17]

Advances in PAP therapy devices have allowed more accurate and intricate data to be recorded and downloaded by the clinician. The introduction of removable data cards and Bluetooth technology has mitigated the reliance on self-reported adherence[11] and rudimentary time meters that only track the amount of time the device was turned on and not the actual usage time. These have been limitations of previous investigations[13,14] and warrant the need for studies examining PAP therapy adherence that use more sophisticated recording devices. Although practice guidelines encourage healthcare providers to use this data as an indicator of treatment adherence and effectiveness, there is limited evidence regarding the outcomes of utilizing this data in healthcare practices.[4]

Currently, OSA treatment guidelines recommend PAP therapy for patients with excessive daytime sleepiness, reduced sleep-related quality of life, or comorbid hypertension.[4] The present study extends these outcomes with the investigation of mortality, hospitalizations, and number of co-morbidities in patients who are adherent and non-adherent to PAP therapy guidelines. Many studies investigating PAP therapy adherence in OSA are also limited by short duration follow-up periods (~3-5 years),[13,15,16,18] and longer observations may be needed for the benefits of PAP adherence to be detected. Such findings may inform the treatment of OSA patients without excessive daytime sleepiness, for whom the current clinical guidelines neither recommend nor contraindicate PAP therapy due to insufficient and inconclusive evidence of reduced CV events and mortality with PAP treatment.

Therefore, the primary objective of this study was to retrospectively compare outcomes such as mortality, hospitalizations, and the development of co-morbidities longitudinally over an eight-year period, between patients with OSA who are adherent and non-adherent to PAP therapy treatment. A secondary objective was to investigate associations of adherence and non-adherence to patient characteristics and outcomes.

METHODS

STUDY DESIGN

The present study is an exploratory longitudinal retrospective randomized chart review of 100 patients with a diagnosis of OSA treated with either continuous PAP (CPAP) or bilevel PAP (BiPAP) therapy. The retrospective nature of the present study excluded its registration as a clinical trial. The chart review included PAP therapy usage from data downloaded from the patient's PAP device during a follow-up visit with a sleep physician at the QEII Health Sciences Centre, Sleep Disorders Clinic (Halifax NS, Canada) between January 1, 2011 and December 31, 2014. The study was given ethical approval from the Nova Scotia Health Authority, Research Ethics Board (REB#1020082).

PARTICIPANT SELECTION

Data downloaded from the patient's device was used to determine PAP therapy adherence. In this study, adherence was defined by an average usage of $\geq$ 4 hours per night on $\geq$ 70% of nights (definition used by Medicare coverage in the US).[8] In order to clearly delineate the adherent and non-adherent groups, non-adherence was defined by an average usage of $\leq$ 3 hours on $\leq$ 50% of nights. Positive airway pressure data were available from 344 patients who had information downloaded to a desktop data management platform during the follow-up period. Of these patients, 213 met the following study eligibility criteria: Inclusion 1) either male or female age $\geq$ 18 years; 2) a clinical diagnosis of OSA (central sleep apnea or hypoventilation could co-exist); 3) treatment with CPAP or BiPAP therapy. Exclusion
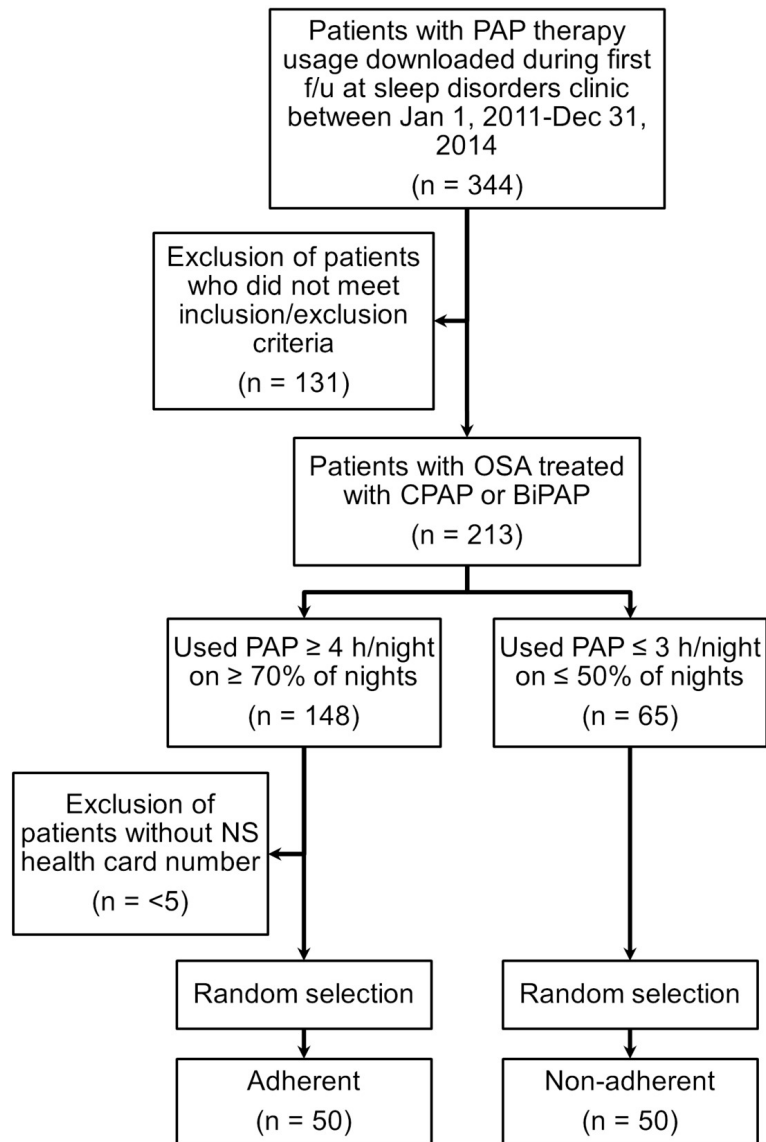
Figure 1. Flow chart of participant selection (CONSORT).

1) diagnosis of a neuromuscular disorder, pure hypoventilation, opioid-related sleep-disordered breathing, or primary complex sleep apnea. All eligible participants were given a unique study identification number and were assigned to either the PAP therapy adherent (n=148; PAP usage ≥ 4 hours on ≥ 70% of nights) or non-adherent (n=65; PAP usage ≤ 3 hours on ≤ 50% of nights) group based on the downloaded PAP usage data. From each group, 50 participants were randomly selected for inclusion in the study using a random number generator and their unique study identification number (Figure 1).

DATA EXTRACTION AND LINKAGE

POSITIVE AIRWAY PRESSURE DEVICE MEMORY CARD

The memory card in each participant's PAP device was downloaded to the EncorePro (version 2.24.0.1, Phillips Respironics) patient data management software. The PAP device download provided usage data over a time period

between the start of PAP therapy and first follow-up appointment (median duration of data download = 273 days). Adherence data collected from the EncorePro software included the date range and duration of the data download, percentage of days with device usage, average usage of all days, average usage of days used, average apnea-hypopnea index, and average time per night in large leak. For participants with multiple PAP device downloads during this time period, the earliest download was selected to determine adherence status since previous studies have shown that early PAP adherence data can be used to predict long-term adherence.[19,20]

CHART REVIEW

Clinical data were manually extracted from paper charts and/or electronic medical records located at the QEII Health Sciences Centre, Sleep Disorders Clinic. Data extracted included date of birth; sex; body mass index; smoking history; tonsil and adenoidectomy; maxillomandibular

advancement surgery; co-morbidities; Epworth Sleepiness Scale (ESS) score; location of start of therapy; time to first follow-up appointment at the Sleep Disorders Clinic; PAP treatment type; and diagnostic information, which included date of diagnosis, method of diagnosis (polysomnography or level III study), apnea-hypopnea index (AHI) or respiratory disturbance index (number of respiratory events per hour), mean oxygen saturation (SpO_2), and minimum SpO_2.

Data were also extracted from the Health Data Nova Scotia (HDNS) databases, which included the Nova Scotia Vital Statistics database from January 1, 2011, to December 31, 2018, to collect data on the date of diagnosis and death and additional information on the cause of death from the Insured Patient Registry from January 1, 2011, to October 31, 2020. Hospital admission, discharge dates and discharge dispositions were collected from the Canadian Institute for Health Information (CIHI) Discharge Abstract Database (DAD) from January 1, 2011 to July 31, 2020. The patient's encrypted Nova Scotia Health Card number (NS-HCN) was used to link the data from the chart review to the HDNS and CIHI databases.

STUDY OUTCOMES

The primary outcome variables for the present study included mortality; hospitalization frequency and duration; and the Charlson Co-morbidity Index (CCI), which is used to predict mortality for patients with several comorbid conditions.[21] Death, cause of death, and date of death were collected from the Vital Statistics database and from the Insured Patient Registry. Hospital admission and discharge dates and discharge dispositions were collected from CIHI -DAD to calculate the length of hospital stay and to identify whether the patient died in hospital. Diagnostic codes and diagnostic types were also collected from the CIHI DAD during the same time-period to calculate the CCI.

STATISTICAL ANALYSES

All statistical analyses were conducted using SAS (Enterprise Guide 8.2). To determine whether significant differences existed between group characteristics and health outcomes of the PAP therapy adherent and non-adherent groups, independent *t*-tests/ Wilcoxon rank sum tests (continuous variables) and Chi-squared/ Fisher Exact tests (categorical variables) were used. Logistic regression was used to identify associations between patient characteristics/ outcomes and PAP therapy adherence. Statistical significance was set *a priori* at $p < 0.05$.

RESULTS

The PAP therapy adherent and non-adherent groups showed good comparability at baseline (Table 1). At the start of PAP therapy treatment, no significant differences were shown for age at time of PAP device data download, sex, body mass index, those classified as obese or non-obese, CCI, smoking history, and past tonsil/ adenoidec-

tomy. However, the PAP therapy adherent group reported a significantly lower ESS score than the non-adherent group at baseline. The method of OSA diagnosis and the number of events/hour were not significantly different between groups, nor was the type of PAP therapy received (BIPAP or CPAP), the location at which therapy was initiated (home/ hospital sleep lab/ other), or time to first follow-up.

Table 2 shows differences in outcomes between the PAP therapy adherent and non-adherent groups over the study's observation period (8 years). No significant differences were shown between the groups for death, death in hospital, number of hospitalizations, length of stay in hospital, and number of co-morbidities over the study duration.

Table 3 shows the results of the logistical regression analysis (PAP therapy adherent versus non-adherent). A significant increase in odds of being adherent to the PAP therapy criteria was shown if the patients were male, while a significant decrease in odds of being adherent was observed in patients reporting higher normal, mild excessive, and severe excessive daytime sleepiness compared to those reporting lower normal daytime sleepiness on the ESS. Logistic regression also showed that an increasing number of hospitalization counts corresponded with a significant decrease in odds of being adherent.

DISCUSSION

Despite widespread usage of PAP therapy in the clinical management of OSA, there is no established definition for the minimum usage of PAP therapy that discerns meaningful patient outcomes.[7] A commonly used definition for PAP therapy adherence is based upon the minimum adherence requirements to receive Medicare coverage in the US, defined as PAP usage of four or more hours per night on 70 percent of nights for at least 30 consecutive days.[8] However, clinical evidence surrounding the validity of this cutoff point in patients with OSA is limited.[7]

Our study showed no significant differences between the PAP therapy adherent and non-adherent groups for mortality, length of stay in hospital, and number of hospitalizations during the eight-year study observation period. However, logistic regression showed that male patients were 8.5-fold more likely to be adherent to PAP therapy than female patients, and patients with a higher normal, mild excessive, and severe excessive daytime sleepiness had significantly lower odds of being adherent compared to patients with lower normal daytime sleepiness. Our data also showed that for every increase in the number of hospitalizations, the odds of being adherent to PAP therapy decreased by approximately 25%.

The criteria to define PAP therapy adherence by the Centres for Medicare and Medicaid Services in the US[8] is seen by many as arbitrary and open to debate, particularly since a dose-response relationship between PAP usage and clinical outcomes in OSA has been reported.[22-25] It has been suggested that specific adherence thresholds may be needed depending on the clinical outcome being investigated.[26] Indeed, Weaver and colleagues showed that despite 4 hours of nightly CPAP therapy being associated

Table 1. Characteristics of the PAP therapy adherent and non-adherent groups.

Characteristic	Adherent (n=50)	% or Std	Non-adherent (n=50)	% or Std	p-value
Age (y)*	59.52	13.10	57.8	12.10	0.400
Sex, male	38	76	29	58	0.056
BMI (kg/m^2)*	36.17	9.10	35.08	8.60	0.746
Obese	37	74	33	66	0.383
Charlson index*	1.08	1.80	0.64	1.00	0.638
Smoking history	32	64	26	52	0.224
Past tonsil/ adenoidectomy	11	22	13	26	0.640
ESS score*	9.21	5.80	11.79	6.00	0.030
OSA diagnosis method					0.880
PSG	16	32	13	26	
PM COMM	23	46	27	54	
PM LAB	7	14	6	12	
Number of events/hour*	43.68	40.40	37.79	27.40	0.552
PAP Treatment type					0.656
BiPAP	13	26	15	30	
CPAP	37	74	35	70	
Location at start of therapy					0.545
Home	29	58	33	66	
Hospital/Lab	20	40	15	30	
Time to first follow up*	22.2	51.60	16.71	23.30	0.814

*Denotes continuous variables; BMI, body mass index; ESS, Epworth Sleepiness; OSA, obstructive sleep apnea; PSG, polysomnography; PM COMM, portable monitoring community; PM LAB, portable monitoring sleep lab; PAP, positive airway pressure; BiPAP, bilevel positive airway pressure; CPAP, continuous airway pressure.

Table 2. Outcomes of the PAP therapy adherent and non-adherent groups during the 8-year study duration.

Characteristic	Adherent (n=50)	% or Std	Non-adherent (n=50)	% or Std	p-value
Death	7	14	<5	<10	0.338
Death in hospital*	6	12	<5	<10	0.269
Number of hospitalizations*	2.9	4.50	3.06	4.20	0.647
Length of stay in hospital (days)*	6.4	10.50	4.48	4.70	0.944
Number of co-morbidities*	3.2	2.00	3.06	2.00	0.769

*Denotes continuous variables

Table 3. Logistic regression analysis (PAP therapy adherent Vs. non-adherent).

	Odds Ratio	95%CI	p-value
Sex (male)	8.519	1.301–55.756	0.025
Epworth Sleepiness Scale Score (Ref – 0-5 (Lower Normal Daytime Sleepiness))			
Higher normal daytime sleepiness (6-10)	0.039	0.005–0.392	0.003
Mild excessive daytime sleepiness (11-12)	0.039	0.003–0.517	0.014
Severe excessive daytime sleepiness (16-24)	0.088	0.012–0.635	0.016
Hospitalization counts	0.741	0.551–0.995	0.046

with improvements in the ESS, 7.5 hours of nightly usage was needed to discern improvements in the Multiple Sleep Latency Test and Functional Outcomes associated with Sleepiness Questionnaire.[22] Furthermore, Faccenda et al. reported that for the treatment of hypertension, CPAP therapy usage of more than 3.5 hours per night is associated with a greater reduction in diastolic blood pressure after four weeks of therapy.[27] In a recent commentary by Javaheri

et al., they suggested that each CV outcome requires a specific minimum number of hours to discern improvements.[28]

Observational studies have found a significant reduction in CV mortality[29] and decreased risk of CV events[30,31] with greater adherence to PAP therapy. However, RCTs have yet to demonstrate PAP therapy efficacy for CV endpoints.[13-15] Indeed, in the Sleep Apnea CV Endpoints (SAVE) study, 2,687 patients with OSA and CV complications were randomized to CPAP therapy or usual care. An intention-to-treat analysis showed a lack of benefit of CPAP therapy for death from any CV cause.[15] For all-cause mortality, several observational studies found that CPAP treatment was significantly associated with reduced mortality compared to no CPAP therapy,[9-12] and CPAP therapy reduced mortality risk to levels similar to patients without OSA.[32] However, RCTs have not shown a significant effect for CPAP treatment on all-cause mortality.[13,15,16] Stringent inclusion/ exclusion criteria used in RCTs may have compromised the generalizability of findings to broader OSA populations. The more lenient eligibility criteria used in this study may have allowed for our results to be more generalizable. Despite this, our study still didn't find significant differences in outcomes between the PAP therapy adherent and non-adherent groups.

The present study supports the findings of previous RCTs regarding the lack of association between PAP therapy adherence and mortality or other clinical outcomes.[13,15,16] The study also agrees with observational studies reporting better adherence to PAP therapy in males than females.[33,34] The CCI was used in the present study to predict mortality for patients with several comorbid conditions. We found no significant difference in CCI between the adherent and non-adherent groups, thus supporting no increased risk of mortality between groups, yet a higher rate of hospitalization was linked with increased non-adherence.

Limitations of this study include the retrospective analysis and small group sample size, which may not have been sufficient to detect a mortality difference. Additionally, many patients in the control group are still using some PAP therapy, which may confer some small benefit compared to no treatment at all. This study may also be confounded by healthy adherer bias,[35] as patients adherent to PAP therapy may also be more likely to adhere to other therapies and healthy behaviours.[36] The strengths of the study include its randomized patient selection, objectively measured PAP therapy usage, broader generalizability, and its eight-year longitudinal follow-up period. The retrospective nature of the study may have also mitigated any strict eligibility criteria used in previous RCTs, making the findings more generalizable to OSA populations.

To the best of the authors' knowledge, this is the first study to investigate the efficacy of the current PAP therapy adherence standard using objectively measured PAP usage data downloaded from the patients' devices and linking them to clinical outcomes. One specific definition for PAP adherence may not be appropriate for the various phenotypes of OSA, where different clinical outcomes will require different usage times and patterns. Consideration should be given to changing the commonly used Centres for Medicare and Medicaid Services definition of adherence for PAP therapy. This exploratory study warrants that further studies be conducted to investigate clinically meaningful criteria for PAP therapy adherence.

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CONTRIBUTORS

DM & KFS conceptualized and designed the study and prepared the REB application, MT was responsible for data extraction, analysis and visualization, and DS wrote the original manuscript. All authors revised the manuscript and reviewed for intellectual content and read and approved the final version.

ETHICAL APPROVAL

All procedures performed in studies involving human participants were in accordance with the ethical standards of the Nova Scotia Health Authority, Research Ethics Board and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. For this type of study, formal consent is not required.

AI STATEMENT

The authors confirm no generative AI or AI-assisted technology was used to generate content.

DISCLAIMER

Portions of the data used in this report were made available by Health Data Nova Scotia of Dalhousie University. Although this research analysis is based on data obtained from the Nova Scotia Department of Health and Wellness, the observations and opinions expressed are those of the authors and do not represent those of either Health Data Nova Scotia or the Department of Health and Wellness.

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