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RESEARCH ARTICLE

Strengthening oropharyngeal muscles as an approach to treat post-stroke obstructive sleep apnea: A feasibility randomised controlled trial

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Summary

This study aimed to determine the feasibility of a randomised controlled trial (RCT) evaluating oropharyngeal exercise (OPE) intervention as an alternative therapy for obstructive sleep apnea (OSA) in patients with stroke or transient ischaemic attack (TIA). Despite the high prevalence of OSA in this population, the standard therapy, continuous positive airway pressure (CPAP), is often poorly tolerated. Thirty stroke/TIA patients with OSA unable to tolerate CPAP were randomly assigned to an oropharyngeal exercise or sham exercise protocol. They performed exercises for 6 weeks, 5 days per week, 30 minutes twice per day. Feasibility was ascertained by the proportion of enrolled patients who completed more than 80% of the OPE regimen. Isometric tongue pressures, apnea–hypopnea index (AHI), oxygen desaturation index (ODI), daytime sleepiness, and quality of life (QOL) outcomes were collected at baseline, post-training (6-week follow-up), and retention (10-week follow-up) to document preliminary efficacy. Adherence to study exercises was excellent, with 83% of participants completing more than 80% of the exercises. The isometric tongue pressures were observed to improve in the oropharyngeal exercise group (compared with the sham group), along with a decrease in OSA severity (measured by the AHI and ODI), reduced daytime sleepiness, and enhanced quality of life outcomes following the exercise programme. Only the effects on posterior isometric tongue pressure and

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daytime sleepiness remained significantly different between groups at the retention session. In conclusion, an RCT evaluating the efficacy of oropharyngeal exercises on post-stroke/TIA OSA is feasible and our preliminary results suggest a clinically meaningful effect.

KEYWORDS
exercise adherence, feasibility, obstructive sleep apnea, oropharyngeal exercises, stroke rehabilitation

INTRODUCTION

Obstructive sleep apnea (OSA) affects ~70% of patients with stroke or transient ischaemic attack (TIA) (Seiler et al., 2019). Obstructive sleep apnea is characterised by recurrent partial or complete collapse of the upper airway during sleep (Jordan et al., 2014). Recurrent collapse of the upper airway exposes the body to harmful physiological stressors such as fluctuations in blood pressure and arousals from sleep (Sánchez et al., 2013). Untreated post-stroke OSA is associated with poorer stroke recovery, reduced quality of life, and longer hospitalisations (Bassetti et al., 2020; Lisabeth et al., 2019; Tomfohr et al., 2012). Despite being associated with adverse health consequences, OSA remains undertreated (Pendharkar et al., 2017). Currently, continuous positive airway pressure (CPAP) is the first-line therapy for treating OSA in stroke/TIA patients (Martínez-García et al., 2009). CPAP provides a pneumatic splint that prevents airway collapse during sleep (Martínez-García et al., 2009). Although CPAP has been shown to be effective at treating post-stroke/TIA OSA, adherence to CPAP in this clinical population is poor (Colelli et al., 2020).

In stroke rehabilitation, oropharyngeal exercises (OPE) are commonly used to improve upper airway muscle function and are associated with improved swallowing (Marzouqah, Huynh, et al., 2023). Previous work has shown a close association between OSA and swallowing impairment due to their common pathogenesis (Losurdo et al., 2018; Shibazaki et al., 2014). Furthermore, electromyography recordings have shown reduced pharyngeal motility and denervation of the upper airway muscles in acute ischaemic stroke patients with swallowing impairments and sleep-disordered breathing, including OSA (Brown et al., 2014; Giannantoni et al., 2016). These findings suggest that oropharyngeal exercise may be effective for managing obstructive sleep apnea in stroke/TIA patients by dealing directly with the underlying pathophysiology of OSA and improving upper airway sensorimotor function to help maintain pharyngeal patency.

The existing literature on oropharyngeal exercise for post-stroke obstructive sleep apnea is limited. Two randomised controlled trials (RCTs) to date have investigated oropharyngeal exercise as a treatment approach for post-stroke obstructive sleep apnea and reported reduced OSA severity and enhanced upper airway muscle function (Qian et al., 2022; Ye et al., 2018). Despite these promising results, there are several limitations to the current literature. Specifically, in the Qian et al. trial (Qian et al., 2022), the treatment group received swallowing therapy techniques alongside OPE, and in the Ye et al. trial, participants using CPAP were not excluded (Ye et al., 2018). As a result, determining the effect of OPE on obstructive sleep apnea severity in both studies becomes challenging. Furthermore, the intervention programmes in both trials included exercises that targeted the muscles outside of the upper airway region (i.e., lips and cheeks); this made some of their exercises unlikely to affect the upper airway region (Marzouqah, Huynh, et al., 2023). Therefore, the effect of oropharyngeal exercise on obstructive sleep apnea deserves further exploration.

Our team developed an oropharyngeal exercise programme to specifically target upper airway muscles, incorporating research findings that employed oropharyngeal exercise to address obstructive sleep apnea and swallowing difficulties (Camacho et al., 2015; Guimarães et al., 2009; Marzouqah, Guaren, et al., 2023; Marzouqah, Huynh, et al., 2023). The programme was designed on the principles of task specificity, emphasising the alignment of exercises with desired outcomes and targeted regions for effective training (Clark, 2012; Kleim & Jones, 2008).

An adequately powered multi-centre randomised controlled trial (RCT) would provide strong evidence for the efficacy of the oropharyngeal exercise programme in reducing obstructive sleep apnea severity in post-stroke/TIA patients. However, before conducting a full RCT, a feasibility trial is recommended to be conducted to demonstrate the feasibility of the intervention and to provide preliminary efficacy data and to identify suitable outcome measures for a larger RCT (Eldridge et al., 2016). In this study, a feasibility trial was conducted to explore the feasibility of the oropharyngeal exercise programme as a treatment strategy for post-stroke/TIA obstructive sleep apnea patients who could not tolerate CPAP. The primary question of this study was whether an RCT of an oropharyngeal exercise regimen would be feasible in stroke/TIA patients with obstructive sleep apnea who were unable to tolerate CPAP. In an exploratory fashion, this study also examined whether an oropharyngeal exercise regimen, compared with sham exercises, would improve patient outcomes.

METHODS

Trial design

A feasibility randomised controlled trial was conducted with a double-blind, parallel group design to investigate the feasibility of an oropharyngeal exercise treatment regimen in treating obstructive sleep

apnea in stroke/TIA patients. Operational procedures, guidelines for the implementation of the interventions, and informed consent were approved by the Sunnybrook Research Ethics Board at Sunnybrook Health Sciences Centre, Toronto, Canada. The registered protocol can be found on ClinicalTrials.gov (Identifier: NCT04212260).

Participants

Participants were recruited by the research team from the Stroke and Sleep Neurology clinic at Sunnybrook Health Sciences Centre. The trial enrolled stroke or TIA patients with OSA, defined by an apnea–hypopnea index (AHI) ≥15 or an AHI ≥5 with a significant oxygen desaturation of 88%, as has been recommended with use of Home Sleep Apnea Testing (HSAT) in stroke/TIA patients (Patel et al., 2018), who were unable to tolerate CPAP after a trial of at least 2 weeks duration. Participants were assessed for obstructive sleep apnea using the MediByte® [Braebon Medical Corporation, Canada], which has been validated for the detection of OSA (Driver et al., 2011).

Inclusion criteria consisted of: (1) no current use of CPAP or oral appliance for sleep; (2) mild to no cognitive impairment (Montreal Cognitive Assessment [MoCA] ≥18); (Nasreddine et al., 2005) (3) absence of oral or apraxia of speech based on the Apraxia Battery for Adults (ABA); (Dabul, 2000) (4) absence of severe aphasia based on the Quick Aphasia Battery; (Wilson et al., 2018) (5) body mass index (BMI) <40 kg/m; (6) absence of craniofacial malformations/nasal obstruction; (7) absence of regular use of hypnotic medication during the 3 weeks preceding study enrollment; (8) absence of a history of neuromuscular disease impacting the oropharyngeal muscles; (9) no use of oxygen therapy (e.g., nasal prongs), a nasogastric tube, or other medical device that would interfere with the use of the home sleep apnea test or overnight pulse oximetry; (10) absence of conditions known to compromise the accuracy of portable sleep monitoring, such as congestive heart failure or pulmonary hypertension (Collop et al., 2007). Baseline characteristics were recorded including demographics (age, sex, neck circumference, smoking history, and BMI), as well as stroke characteristics including location, type, and time since stroke. Baseline orofacial sensorimotor function was also assessed using the Frenchay Dysarthria Assessment (FDA-2) (Enderby, 1980).

Study procedures

The oropharyngeal exercise protocol consisted of six exercises targeting the upper airway muscles, while the sham control protocol consisted of six mouth and tongue movements (see Supplementary File S1 for the list of exercises). Both protocols were delivered via a tablet-based Android application (app) called OPEX (Marzouqah, Pommée, et al., 2023). The app included video recorded instructions and demonstrations of each exercise as well as a daily log of exercises. Participants performed the exercises for 6 weeks, 5 days per week, twice daily for 30 min at a time (~1800 min in total). The app stored all the videos completed by the participants to estimate exercise compliance (i.e., exercising time). Participants were trained at the beginning of the programme to do the exercises independently at home by a speech-language pathologist (SLP). Prespecified follow-up audio and/or video calls were performed weekly to provide retraining and to troubleshoot technical issues.

Once the participants finished the 6 weeks of training, they completed the post-training assessments. They were then instructed to stop doing the exercises for 4 weeks. After this 4-week break, they completed the retention assessments, which assessed the long-term effects gained from the training programme.

Primary outcome measure

The primary goal of the present study was to determine the feasibility of the oropharyngeal exercise treatment regimen in stroke and TIA patients with obstructive sleep apnea, thus, the primary outcome was participant adherence. Participant adherence to the study exercises in both groups was assessed by measuring exercise duration in minutes through the app. Research assistants reviewed recorded videos to confirm exercise sessions. Video titles were then used to extract session details, including session number, exercise duration, and time, enabling calculations of total sessions, time per session, and total exercising duration. The oropharyngeal exercise regimen was considered feasible if at least 80% of eligible patients completed more than 80% of the study exercises. The number of patients screened and ultimately recruited for the study was also tracked.

Secondary outcome measures

To determine preliminary efficacy, the following secondary outcomes were obtained at baseline, post-training (6 weeks), and retention (10 weeks): (1) Obstructive sleep apnea severity was measured by the AHI, assessed by the home sleep apnea test, MediByte® (Driver et al., 2011). The test encompassed several physiological channels, including respiratory effort, pulse, oxygen saturation (SpO_2), nasal flow, snoring, and body position channels. The scoring criteria for apneas and hypopneas were events lasting ≥10 s, apneas being defined by a ≥90% drop in airflow and hypopneas being characterised by a ≥30% reduction in airflow associated with a ≥4% drop in oxygen saturation (Berry et al., 2017). (2) Oxygen desaturation index (ODI), also assessed by the home sleep apnea test; desaturations were identified as instances of oxygen saturation dropping by ≥4% (Berry et al., 2017). (3) Patient-reported sleep-related symptoms, assessed by the Functional Outcomes of Sleep Questionnaire (FOSQ) (Weaver et al., 1997), Epworth Sleepiness Scale (ESS) (Johns, 1991), and the Fatigue Severity Scale (FSS) (Krupp, 1989). (4) Functional and quality of life outcomes, assessed by the Stroke Impact Scale (SIS) (Duncan et al., 2003). (5) Anterior and posterior isometric tongue pressures were measured using the Iowa Oral Performance Instrument (IOPI), a handheld manometry device with a teaspoon-sized air-

filled bulb placed on the tongue's upper surface (Adams et al., 2013). The device recorded the displaced air in kilopascals when the bulb was compressed. Anterior placement positioned the bulb just behind the front upper teeth, while posterior placement aligned it with the anterior edge of the first molar. Participants were instructed to press the bulb with maximum tongue pressure, and the average of three trials was calculated.

Randomisation and blinding

Study allocation (i.e., oropharyngeal vs. sham exercises) was randomly assigned using simple randomisation with a ratio of 1:1. After completing the informed consent form and baseline measures, participants were randomised using a password-protected Excel sheet with random numbers (1 or 2). "1" corresponded to tablets that were pre-programmed to deliver oropharyngeal exercises and "2" corresponded to tablets that were pre-programmed to deliver sham exercises. The SLP who trained the patients on the exercises was the only person who had access to participants' randomisation status. Study intervention assignments remained concealed from outcome assessors, participants, the study investigators, and the on-site research assistants.

Statistical analysis

To follow the intention-to-treat (ITT) principle, all participants were included in the analysis regardless of their status at the end of the study. For our descriptive statistics, continuous variables were reported as means and standard deviations and categorical variables as frequency counts and percentages. To assess the primary outcome, the percentage and total training hours were computed for each participant. For participants who dropped out, the total number of hours of exercise completed before leaving the study was used in our analyses. The percentage and mean of total training hours were computed for each group with 95% confidence intervals. A linear regression model was used to explore whether pre-specified predictors (i.e., age, sex, time since stroke) were correlated to OPE regimen completion. For our secondary outcomes, linear regression models, adjusting for the baseline score (ANCOVA), were used to compare our secondary outcomes between the study arms at post-training and retention. Predictive model-based multiple imputation was used to impute missing data using the multivariate imputation by chained equations (mice) package (White et al., 2011) in the R software (R Core Team, 2023). The models were first fitted unconditionally (without covariates) and then the baseline values of sex, age, and time since stroke/TIA were used as covariates. The treatment effect was reported as the adjusted mean difference with 95% CI and the significance level was set at $p < 0.05$.

Sample size

As this is a feasibility study, it would not be customary to perform a sample size calculation or formal power analysis. Nevertheless, we considered the sample size calculation was based on the secondary outcome, AHI. Based on a previous study that examined oropharyngeal exercises, the expected standard deviation of the AHI was 8.5 events/per hours (Guimarães et al., 2009). The planned sample size of 20 per group would have 80% power to detect a difference between groups of an AHI of 7.8, using a *t*-test with a two-sided alpha of 5%. The analytic method used in this study (regression, adjusted for baseline ANCOVA) was more powerful, meaning that the study could detect the proposed or a slightly smaller treatment effect with a smaller sample size (Borm et al., 2007).

RESULTS

Baseline data

The baseline demographic and clinical characteristics of the participants were comparable across the groups, as shown in Table 1. All participants demonstrated obstructive sleep apnea rather than central sleep apnea (CSA) throughout the study, as indicated in Table 2.

Recruitment and participant flow

Recruitment was slower than anticipated and was stopped after randomisation of 30 stroke/TIA patients after 35 months of recruitment (December 2019 to November 2022). During this period, 76 participants with stroke or TIA were screened, of whom 54 (71%) were eligible and 30 (56%) consented to participate. The main reasons for exclusion were opting to retry CPAP ($n = 11$; 46%) and declining to participate ($n = 10$; 42%). Of the 30 consented participants, $n = 24$ (80%) completed all assessments except for the isometric tongue pressure measures. Because of the SARS-CoV-2 outbreak, only 16 participants managed to complete isometric tongue pressure measurements, as accessing the hospital became challenging due to concerns about virus transmission. Figure 1 shows the CONSORT flow diagram.

Adherence to the study intervention

Adherence to the exercise regimens was excellent, as 25 out of 30 (83.33%) participants completed more than 80% of the exercise programme (Figure 2) and both exercise groups showed mean adherence rates >80% (Table 3). The results from the linear regression model showed that there were no associations between exercise adherence (total exercising hours) and predictor variables (i.e., group assignment, age, gender, time since stroke or TIA, AHI, and cognitive score) (Table 4).

Efficacy

Table 5 summarises the statistical results of the final best-fit models examining the impact of the oropharyngeal exercise

TABLE 1 Participant demographics.

	Total ($N = 30$)	OPE group ($N = 15$)	Sham group ($N = 15$)
Age in years, mean (SD)	67.3 (11.4)	66.7 (11.4)	68.0 (11.8)
Male, *N* (%)	19 (63%)	11 (73%)	8 (53%)
BMI, mean (SD)	28.7 (7.5)	29.1 (9.3)	28.2 (5.5)
Neck circumference in cm, mean (SD)	17.3 (6.0)	16.5 (2.3)	17.7 (7.5)
Montreal cognitive assessment, mean (SD)	24.4 (4.6)	24.4 (4.5)	24.3 (4.3)
Years of education, mean (SD)	16.7 (3.0)	16.5 (2.7)	16 (3.4)
Stroke (opposed to TIA), *N* (%)	23 (77%)	12 (80%)	11 (73%)
Ischaemic stroke (opposed to haemorrhagic), *N* (%)	28 (93%)	14 (93%)	14 (93%)
Time since stroke or TIA in months, mean (SD)	21 (18.1)	20 (20.3)	21.5 (16)
Location of stroke or TIA, *N* (%)			
Supratentorial	25 (83%)	13 (86%)	12 (80%)
Infratentorial	2 (6%)	1 (6%)	1 (8%)
Both	3 (11%)	1 (8%)	2 (13%)
Smoking, *N* (%)			
None	20 (66%)	9 (60%)	11 (73%)
Prior	7 (23%)	4 (26%)	3 (20%)
Current	3 (11%)	2 (14%)	1 (7%)
Dysarthria, *N* (%)			
None	29 (96%)	14 (93%)	15 (100%)
Mild dysarthria	1 (4%)	1 (7%)	0 (0%)
Aphasia, *N* (%)			
None	29 (96%)	12 (93%)	15 (100%)
Mild aphasia	1 (4%)	1 (7%)	0 (0%)

Abbreviations: OPE, oropharyngeal exercises; SD, standard deviation; TIA, transient ischaemic attack.

TABLE 2 Obstructive and central sleep apnea indicators among participants at baseline, post-training, and retention, mean (SD).

Group	Time point	Apnea–hypopnea index (AHI)	Obstructive apnea index	Central apnea index	Supine apnea–hypopnea index	Non-supine apnea–hypopnea index	Oxygen desaturation index (ODI) 4%	Oxygen saturation levels (SpO_2)	% of Sleep time with oxygen saturation below 90% ($t < 90\%$)
OPE	Baseline ($N = 15$)	24.8 (8.0)	12.8 (1.80)	2.7 (0.85)	36.3 (5.80)	9.8 (4.20)	25.3 (11.6)	91.3 (0.57)	23.5 (7.88)
	Post-training ($N = 14$)	14.6 (9.8)	6.8 (1.76)	0.7 (0.37)	21.1 (5.03)	6.1 (1.57)	12.6 (8.5)	94.2 (0.92)	15.1 (8.52)
	Retention ($N = 13$)	23.7 (9.5)	11.2 (1.74)	2.1 (0.50)	34.4 (4.87)	9.7 (3.51)	23.2 (8.8)	91.1 (0.73)	21.2 (8.76)
Sham	Baseline ($N = 15$)	17.8 (9.4)	8.5 (1.77)	1.1 (0.50)	27.5 (6.15)	9.4 (1.92)	18.0 (13.5)	90.0 (0.34)	20.5 (3.84)
	Post-training ($N = 14$)	16.7 (10.7)	7.9 (2.07)	1.9 (0.66)	28 (5.39)	7.5 (2.60)	16.2 (11.5)	92.1 (0.77)	19.1 (3.90)
	Retention ($N = 13$)	15.7 (8.7)	8.6 (1.75)	1.6 (0.58)	26.5 (7.24)	10.1 (2.75)	14.0 (11.1)	93.0 (0.35)	19.9 (6.31)

Abbreviation: OPE, oropharyngeal exercises.

intervention on the secondary outcomes, compared with the sham intervention. The mean AHI at post-training was significantly lower for patients in the oropharyngeal exercise arm, compared with the sham arm, with an estimated effect of −12.1 ([95% CI, −23.0 to −1.2], $p = 0.031$). There were no demonstrated differences in mean AHI between both groups at retention. Similarly, the oxygen desaturation index was significantly lower in the oropharyngeal exercise group with a group difference of −10.7 at post-training ([95% CI, −18.1 to −3.3], $p = 0.011$) but not at retention. The oropharyngeal exercise group demonstrated significantly lower levels of daytime sleepiness, as measured by the Epworth sleepiness scale, with estimated effects of −4.0 [95% CI, −6.3 to −1.6], $p = 0.002$ at post-training, and −3.7 [95%CI, −5.6 to −4.1], $p = 0.005$ at retention. There were no demonstrable differences in the other sleep and fatigue questionnaires between study arms at post-training or retention. The Stroke Impact Scale results

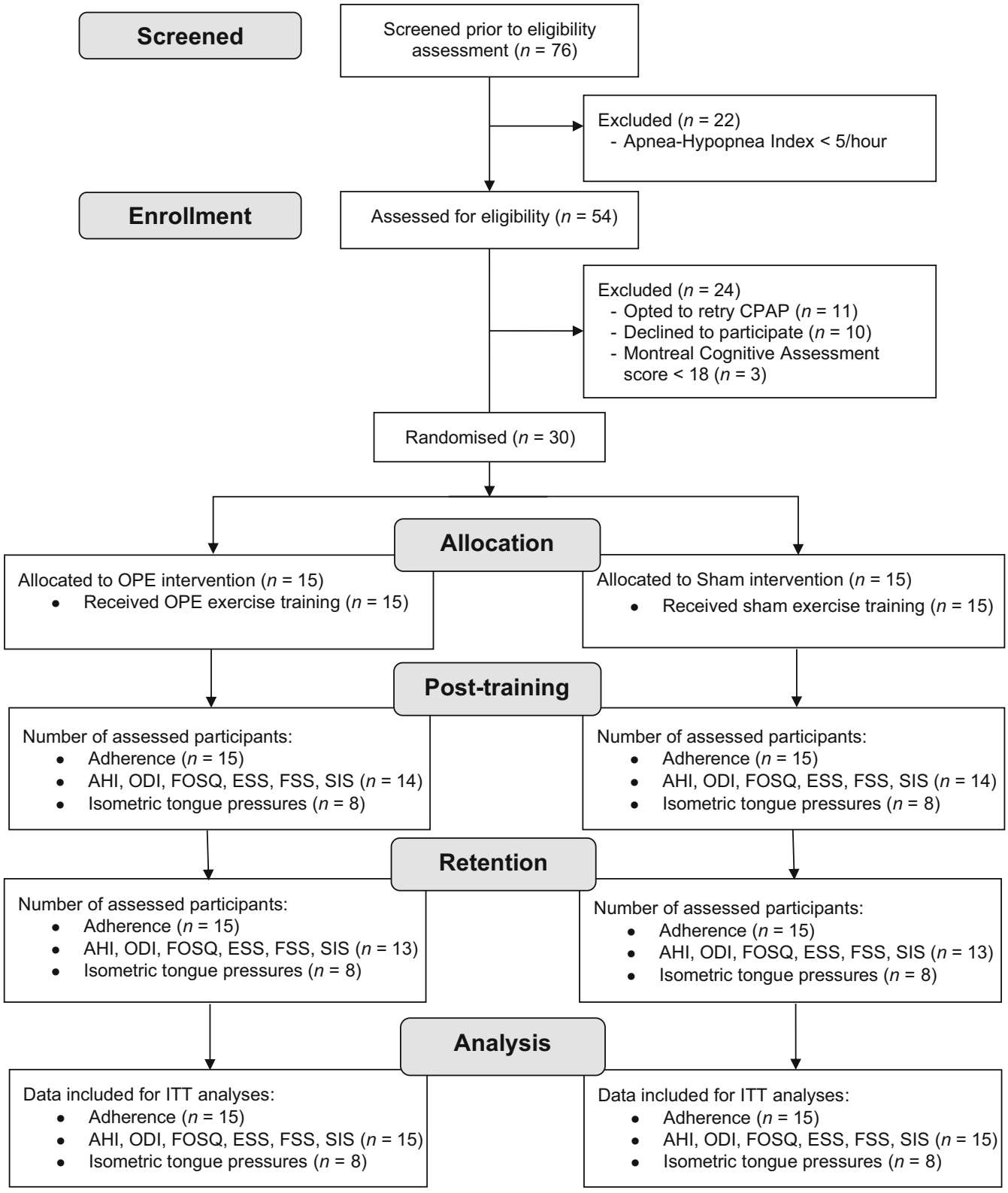

FIGURE 1 CONSORT flow diagram. AHI, apnea–hypopnea index; CPAP, continuous positive airway pressure; ESS, Epworth sleepiness scale; FSS, fatigue severity scale; FOSQ, functional outcomes of sleep questionnaire; ITT, intention-to-treat; OPE, oropharyngeal exercises; ODI, oxygen desaturation index; SIS, stroke impact scale.

showed that the oropharyngeal exercise group demonstrated significant improvements compared with the sham group in several subscales at post-training, including strength (22.7 [95% CI, 1.3–44.1], $p = 0.039$), communication (20.5 [95% CI, 0.2–40.8], $p = 0.048$), activities (12.7 [95% CI, 2.6–22.7], $p = 0.016$), mobility (15.5 [95% CI, 2.78–28.2], $p = 0.019$), and social participation (13.1 [95% CI, 5.39–40.7], $p = 0.013$). There was weaker evidence for group differences at retention. Other components of the

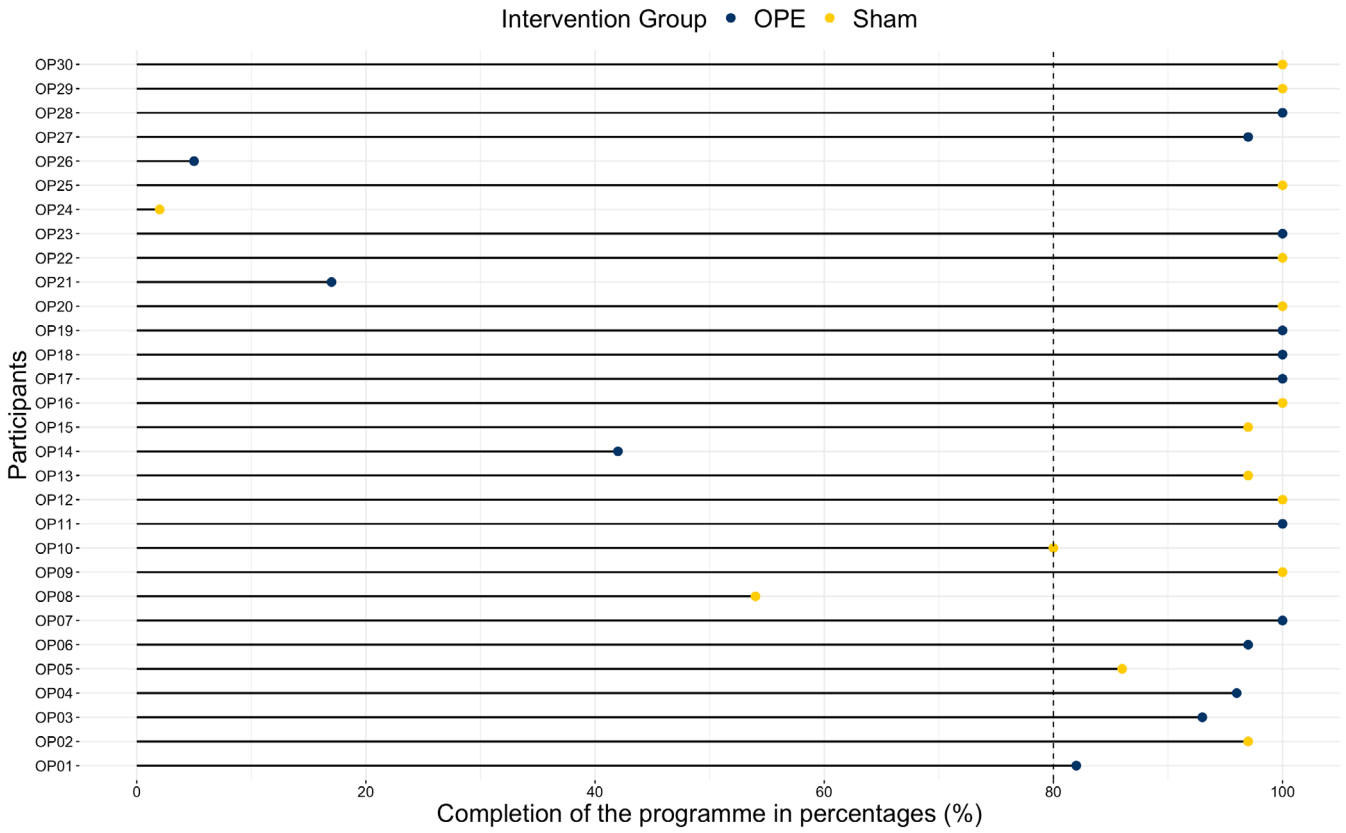

FIGURE 2 Percentage of exercise programme completion in both groups. OPE, oropharyngeal exercises.

TABLE 3 Adherence to study exercises.

	OPE group	Sham group	Both groups
Total exercising hours, minutes, mean [95% CI], %	1587.9 [95% CI, 1338.3–1737.7], 88%	1517.6 [95% CI, 1184.4–1750.8], 84%	1551.58 [95% CI, 1354.2–1748.8], 86%
Additional adherence parameters			
Number of completed sessions, mean [95% CI]	54.8 [95% CI, 41.2–60.0]	55.5 [95% CI, 35.2–60.0]	55.6 [95% CI, 31.8–60.0]
Time per session, minutes, mean [95% CI]	28.9 [95% CI, 25.5–30.0]	27.2 [95% CI, 24.1–30.0]	27.8 [95% CI, 24.6–30.0]

Abbreviations: CI, confidence interval; OPE, oropharyngeal exercises.

TABLE 4 Predictors of exercise adherence (total exercising hours).

	Exercise adherence		
Predictor variables	Standardised beta coefficient	95% confidence intervals	*p*-value
Group (sham as a reference)	−0.07	−92.0 to 92.0	0.730
Age	−0.05	−26.1 to 26.0	0.984
Sex (Male as a reference)	0.20	−11.0 to 11.0	0.391
Time since stroke/TIA	−0.34	−9.0 to 8.8	0.124
Apnea–hypopnea index	−0.04	−10.0 to 11.0	0.753
Cognitive score	−0.07	−25.0 to 25.0	0.804

Abbreviation: TIA, transient ischaemic attack.

Stroke Impact Scale did not show meaningful differences between study arms at either the post-training or retention sessions.

Table 6 summarises the statistical results of the sub-sample ($n = 16$) that completed the isometric tongue pressure assessments. There was a statistically significant improvement in anterior pressure in the oropharyngeal exercise group compared with the sham group at post-training (10.6 [95% CI, 6.51–14.7], $p = 0.001$). Additionally, there was a trend indicating an oropharyngeal exercise intervention effect on anterior tongue pressure at retention; however, this effect did not reach significance. In contrast, the results for the posterior isometric tongue pressure showed a significant oropharyngeal exercise intervention effect at each visit: post-training (12.8 [95% CI, 7.58–18.1], $p = 0.002$) and retention (10.9 [95% CI, 1.5–21.2], $p = 0.040$).

TABLE 5 Sleep and stroke outcomes: baseline, post-training, and retention ($n = 30$).

	OPE group			Sham group			Estimated effect with 95% CI for post-training (p value)	Estimated effect with 95% CI for retention (p value)
	Baseline	Post-training	Retention	Baseline	Post-training	Retention		
Apnea–hypopnea index	24.8 (8.0)	14.6 (9.8)	23.7 (9.5)	17.8 (9.4)	16.7 (10.7)	15.7 (8.7)	−12.1 [−23.0 to −1.2] $\mathbf{p = 0.031}$*	2.4 [−8.7 to 13.7] $p = 0.65$
Oxygen desaturation index	25.3 (11.6)	12.6 (8.5)	23.2 (8.8)	18.0 (13.5)	16.2 (11.5)	14.0 (11.1)	−10.7 [−18.1 to −3.3] $\mathbf{p = 0.011}$*	1.3 [−7.41 to 10.1] $p = 0.75$
Epworth sleepiness scale	7.4 (4.1)	3.54 (2.3)	3.8 (2.7)	5.2 (3.9)	6.18 (4.7)	5.9 (4.5)	−4.0 [−6.3 to −1.6] $\mathbf{p = 0.002}$*	−3.7 [−5.6 to −4.1] $\mathbf{p = 0.005}$*
Functional outcomes of sleep questionnaire	3.5 (0.4)	3.4 (0.6)	3.5 (0.4)	3.4 (0.5)	3.3 (0.6)	3.3 (0.5)	−0.001 [−0.5 to −0.01] $p = 0.992$	0.1 [−0.4 to 0.5] $p = 0.700$
Fatigue severity scale	3.5 (1.4)	3.3 (1.6)	2.9 (1.5)	3.8 (1.9)	3.8 (2.1)	4.0 (2.1)	−0.2 [−1.5 to 1.1] $p = 0.772$	−0.8 [−2.1 to 0.5] $p = 0.208$
Stroke impact scale								
Strength	74.5 (28.9)	86.1 (24.0)	80.8 (30.1)	72.4 (19.1)	65.9 (27.3)	71.0 (29.5)	22.7 [1.3–44.1] $\mathbf{p = 0.039}$*	14.1 [−9.2 to 37.5] $p = 0.225$
Memory	76.7 (28.6)	80.8 (25.3)	86.1 (20.9)	84.3 (14.7)	75.3 (22.5)	83.8 (18.1)	9.7 [−8.0 to 27.5] $p = 0.268$	5.5 [−9.5 to 20.4] $p = 0.458$
Emotion	85.6 (18.3)	92.7 (13.4)	93.1 (13.2)	90.9 (13.8)	84.5 (19.5)	88.6 (16.1)	11.1 [−1.01 to 23.2] $p = 0.070$	6.2 [−5.8 to 18.2] $p = 0.293$
Communication	74.2 (31.4)	85.4 (24.9)	85.4 (23.1)	82.4 (30.2)	80 (34.5)	76.8 (35.0)	20.5 [0.2–40.8] $\mathbf{p = 0.048}$*	13.7 [−6.0 to 22.4] $p = 0.164$
Activities	86.0 (13.9)	92.3 (11.7)	92.3 (13.8)	90.6 (10.5)	82.5 (15.8)	88.6 (11.0)	12.7 [2.6–22.7] $\mathbf{p = 0.016}$*	6.3 [−2.97 to 15.6] $p = 0.172$
Mobility	79.1 (16.3)	91.8 (13.1)	85.7 (20.4)	85.1 (20.3)	79.2 (20.6)	76.9 (19.3)	15.5 [2.78–28.2] $\mathbf{p = 0.019}$*	12.8 [−0.9 to 26.5] $p = 0.065$
Hand function	70.3 (15.3)	75.2 (11.2)	77.8 (9.5)	71.5 (6.8)	66.9 (19.8)	69.4 (20.6)	9.0 [−2.94 to 21.0] $p = 0.132$	8.9 [−3.4 to 21.3] $p = 0.145$
Social participation	71.8 (30.6)	84.9 (26.1)	84.4 (29.0)	74.4 (30.8)	74.4 (33.5)	72.2 (32.4)	13.1 [5.39–40.7] $\mathbf{p = 0.013}$*	13.9 [−6.4 to 34.2] $p = 0.170$
Overall recovery	90.9 (15.0)	91.8 (14.5)	89.4 (16.3)	80.3 (24.1)	79.6 (28.6)	77.5 (29.0)	2.6 [−3.1 to 8.3] $p = 0.358$	−1.75 [−8.22 to 4.75] $p = 0.581$

Abbreviations: CI, confidence interval; OPE, oropharyngeal exercises.
*The significance level was set at $p < 0.05$.

TABLE 6 Isometric tongue pressure outcomes: baseline, post-training, and retention ($n = 16$).

	OPE group			Sham group			Estimated effect with 95% CI for post-training (p value)	Estimated effect with 95% CI for retention (p value)
	Baseline	Post-training	Retention	Baseline	Post-training	Retention		
Anterior isometric tongue pressures	34.7 (6.5)	40.4 (5.8)	35.8 (6.44)	35.1 (9.1)	30.5 (6.3)	31.7 (9.2)	10.6 [6.5–14.7] $\boldsymbol{p = 0.001}$*	2.8 [−4.9 to 10.6] $p = 0.195$
Posterior isometric tongue pressures	33.7 (7.8)	41.6 (3.1)	37.0 (4.4)	32.2 (8.9)	29.5 (7.5)	28.8 (11.3)	12.8 [7.5–18.1] $\boldsymbol{p = 0.002}$*	10.9 [1.5–21.2] $\boldsymbol{p = 0.040}$*

Abbreviations: CI, confidence interval; OPE, oropharyngeal exercises.
*The significance level was set at $p < 0.05$.

DISCUSSION

This study demonstrated that an RCT evaluating the effect of oropharyngeal exercise on post-stroke/TIA obstructive sleep apnea was feasible. Most of the participants demonstrated high compliance with the exercise treatment programme. The study also showed that the oropharyngeal exercise group demonstrated a reduction in OSA severity, reduced daytime sleepiness, and enhanced functional outcomes immediately after the exercise regimen, compared with the sham group. The improvements in isometric tongue pressure underlined these functional changes in a subgroup of participants. Gains in posterior tongue pressures and reduced daytime sleepiness remained significant following the no-exercise period.

The oropharyngeal exercise programme demonstrated strong participant compliance, with an average adherence rate of 86% (OPE: 88%; sham: 84%). Ye et al. (2018) reported similar adherence rates ranging from 81.5% to 100% in post-stroke patients with a comparable OPE programme duration (20 min) (Ye et al., 2018). This is particularly promising when contrasted with the low 50% adherence reported for CPAP in post-stroke OSA (Colelli et al., 2020). The use of the OPEX app in our study may have positively influenced exercise adherence, as previous research has highlighted improved compliance with exercises when utilising apps (Lambert et al., 2017). Future research with a larger sample size is needed to examine further the factors affecting adherence in oropharyngeal exercise programmes.

The intended sample was 40 post-stroke/TIA patients with obstructive sleep apnea. However, due to challenges such as the declaration of the SARS-CoV-2 pandemic in the middle of the study (Cucinotta & Vanelli, 2020) and difficulties recruiting patients who met our strict inclusion criteria, recruitment was halted after enrolling 30 participants over 35 months. Despite this, our study was unique in evaluating both post-training and retention effects, distinguishing it from previous OPE-based research on stroke obstructive sleep apnea (Qian et al., 2022; Ye et al., 2018). Remarkably, 80% ($n = 24$) of participants attended all assessment sessions. With the insights gained from this feasibility trial, the study team is well positioned to advance to an efficacy trial to further explore the effect of the oropharyngeal exercise programme on obstructive sleep apnea.

The current exercise programme included specific exercises for the upper airway and was designed based on guidelines from exercise and neurorehabilitation research that emphasise the importance of specificity in exercise training (Kleim & Jones, 2008). In contrast to prior studies that incorporated functional activities such as oral breathing and swallowing in the oropharyngeal exercise programme (Guimarães et al., 2009; Ye et al., 2018), our programme did not include these activities, prioritising task specificity (Clark, 2012; Kleim & Jones, 2008; Marzouqah, Huynh, et al., 2023). There is a minor likelihood that this exclusion might have influenced our retention results, considering the reported links between oral breathing, swallowing, and obstructive sleep apnea (Lee et al., 2007; Pizzorni et al., 2021). Unfortunately, due to the absence of reported long-term results in studies that incorporated functional activities, the long-term benefits remain unclear (Camacho et al., 2015). Moreover,

variations in exercise protocols and non-standardised oropharyngeal assessments challenge current OPE-based OSA research (Marzouqah, Huynh, et al., 2023). To improve our understanding, future studies should evaluate oropharyngeal exercise programmes using standardised assessments over extended follow-ups.

The present results align with previous studies on oropharyngeal exercise for post-stroke OSA, demonstrating benefits in oropharyngeal motility, OSA severity, and functional outcomes in the treatment group (Qian et al., 2022; Ye et al., 2018). When oropharyngeal exercise is placed alongside other interventions, such as CPAP – which is known to be effective in improving stroke outcomes with CPAP adherence for ≥4 h per night (Boulos et al., 2021) – the oropharyngeal exercise programme may serve as a potential alternative therapy for cases of low/non-CPAP adherence. An oral appliance, designed to improve upper airway dynamics through alteration of jaw and tongue position during sleep, has showed positive outcomes in non-stroke individuals with mild to severe obstructive sleep apnea (Sutherland et al., 2014), yet its effects on post-stroke obstructive sleep apnea deserves further exploration (Bassetti et al., 2020).

Current guidelines do not mention the use of oropharyngeal exercise for managing OSA, however, emerging evidence suggests that OPE interventions may be beneficial for treating obstructive sleep apnea (Camacho et al., 2015; Rueda et al., 2020). In addition, current research on OSA phenotyping suggests that OPE therapy may play a role in the mainstream treatment of obstructive sleep apnea, specifically for individuals with low muscle responsiveness (Eckert, 2018). Nevertheless, practitioners must consider not only the therapy's merits but also a patient's motivation, lifestyle, and socioeconomic factors to recommend the most appropriate intervention (Almeida et al., 2013). Future research should prioritise personalised medicine approaches within the context of post-stroke OSA.

The present study had several limitations. First, most of the sample consisted of patients with chronic strokes of mild severity. This made it difficult to elucidate the direct relationship between stroke characteristics and obstructive sleep apnea, and to determine whether obstructive sleep apnea manifested before or after stroke. This was deemed acceptable as the study's primary focus was on feasibility and exercise adherence, rather than delving into this bidirectional relationship often described as a "chicken-or-egg" relationship in the literature (Alexiev et al., 2018; Bassetti et al., 2020). Nonetheless, the inclusion of participants with mild severity strokes and TIA was deliberate. Earlier studies have highlighted that the prevalence of obstructive sleep apnea in TIA patients parallels that seen in stroke patients (Johnson & Johnson, 2010; Seiler et al., 2019). Given the current success of the oropharyngeal exercise programme in addressing OSA symptoms among stroke/TIA patients with mild stroke events, this exercise programme may be generalisable to patients without a history of stroke. Another limitation is that the study did not reach the planned sample size. However, the given nature of the ANCOVA test, this study was able to detect group differences with a smaller sample size. Finally, the adherence analysis was focussed only on the study period (6 weeks), but long-term adherence to the exercise programme should be explored in future research.

CONCLUSIONS

This study determined that a randomised controlled trial evaluating the effect of OPE on post-stroke obstructive sleep apnea was feasible. Despite the slow recruitment rates, participants showed high adherence to the oropharyngeal exercise programme, which was notably greater than the adherence seen with CPAP therapy for post-stroke OSA. In patients with stroke/TIA, the use of oropharyngeal exercise has the potential to reduce OSA severity, daytime sleepiness and to improve functional outcomes. The effects of oropharyngeal exercise on posterior tongue pressures and daytime sleepiness maintained for 4 weeks without exercising. The implications of this study could lead to the development of a well-tolerated alternative to CPAP for obstructive sleep apnea management after stroke/TIA, ultimately improving patient outcomes and quality of life.

AUTHOR CONTRIBUTIONS

Reeman Marzouqah: Funding acquisition; writing – original draft; writing – review and editing; formal analysis; project administration; data curation; investigation; visualization. **Laavanya Dharmakulaseelan:** Investigation; writing – review and editing; project administration; data curation. **David R. Colelli:** Project administration; writing – review and editing; data curation. **C. J. Lindo:** Writing – review and editing; project administration. **Yakdehikandage S. Costa:** Writing – review and editing; project administration. **Trevor Jairam:** Writing – review and editing; project administration. **Kathy Xiong:** Writing – review and editing; project administration. **Brian J. Murray:** Writing – review and editing; supervision; resources. **Joyce L. Chen:** Methodology; writing – review and editing; supervision. **Kevin Thorpe:** Formal analysis; supervision; writing – review and editing. **Yana Yunusova:** Conceptualization; funding acquisition; writing – review and editing; methodology; investigation; project administration; supervision; resources; validation; writing – original draft. **Mark I. Boulos:** Conceptualization; investigation; funding acquisition; writing – original draft; methodology; writing – review and editing; resources; supervision; project administration; formal analysis.

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CONFLICT OF INTEREST STATEMENT

The authors declare that they have no non-financial conflicts of interest related to this manuscript.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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