#### ORIGINAL RESEARCH





# Relationship between SDB and short-term outcome in Finnish ischemic stroke patients

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#### **Abstract**

**Objectives:** Presence of sleep-disordered breathing (SDB) affects negatively recovery from stroke. The aim of this study is to evaluate the relationships between sleep-disordered breathing (SDB) and outcome measures in Finnish stroke unit cohort: mRS, need of rehabilitation and hospitalization time.

Material and Methods: An observational longitudinal study consisted of 95 patients referred to the Stroke Unit of Satakunta Hospital District over a period of November 2013 to March 2016. Patients were tested for SDB within 72 hr from the hospital admission because of ischemic stroke or TIA. The patients underwent polysomnography with NOX T3 wireless recorder.

**Results:** There are 37% (n = 35) non-OSA patients, 20% (n = 19) of patients have mild obstructive sleep apnea (OSA) and 39% (n = 37) have moderate/severe OSA and 4% (n = 4) have CSA. Patients with OSA have higher proportion of disability scores of mRS 3–5 (38%) compared to non-OSA (11%) and mild OSA (5%) patients on registration day (mRSO), and the same trend is seen at hospital discharge 35% versus 9% and 5%. (p = .009). Proportion of patients with OSA who needed rehabilitation is 65% (n = 19) versus non-OSA patients 17.5% (n = 4) and mild OSA patients 17.5% (n = 4; p = .039). We observed longer duration of hospitalization (5–15 days) in 29% of OSA patients compared to mild OSA patients 47% and OSA patients 54%. (p = .045).

**Conclusion:** Ischemic stroke patients with OSA have higher disability, higher need of rehabilitation, and longer hospitalization length. Prescreening tools for recognizing these stroke patients in acute phase could be valuable. That could result in earlier initiation of treatment and might prevent worse recovery from stroke.

#### KEYWORDS

ischemic stroke, obstructive sleep apnea, outcome

# 1 | INTRODUCTION

Sleep-disordered breathing (SDB) is frequent among ischemic stroke and TIA patients and several studies have estimated the prevalence between 50% and 70% depending on the definition (Bassetti &

Aldrich, 1999; Bassetti, Aldrich, Chervin, & Quint, 1996; Hermann & Bassetti, 2009, 2016; Sahlin et al., 2008). In stroke care, SDB and especially the most common condition, obstructive sleep apnea (OSA) is preceding condition and a known risk factor for ischemic stroke (European Stroke Organisation (ESO) Executive Committee and

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ESO Writing Committee, 2008; Yaggi et al., 2005; Young, Peppard, & Gottlieb, 2002). Recurrent hypoxemia, variable blood pressure, increased cardiac arrhythmias, and cerebral hypoperfusion caused by SDB may contribute to higher disability from stroke (Hermann and Bassetti, (2009); Sahlin et al., 2008; Bassetti & Aldrich, 1999; Somers et al., 2008; Somers, Dyken, Clary, & Abboud, 1995; Urbano, Roux, Schindler, & Mohsenin, 2008). Additionally, sleep disorders impair daytime wakefulness, cognitive functions, and mood which in negative way influence rehabilitation, worsens the outcome and quality of life and prolongs hospitalization (Good, Henkle, Gelber, Welsh, & Verhulst, 1996; Hermann & Bassetti, 2009; Kaneko, Hajek, Zivanovic, Raboud, & Bradley, 2003; Moyer, Sonnad, Garetz, Helman, & Chervin, 2001). Higher rate of recurrent cardiovascular events and mortality have observed in patients with SDB in several studies (Hermann & Bassetti, 2016; Parra et al., 2004; Sahlin et al., 2008: Young et al., 2002).

SDB can be diagnosed by overnight polysomnography but a simpler and portable version, respiratory polygraphy which is used in this study, is considered as a sufficient method for diagnosing SDB (Erkinjuntti, Salmi, Polo, & Kirjavainen, 2006; Collop et al., 2007; Parra et al., 1997). There are only few studies of the prevalence of SDB and in Finnish stroke patients and sleep recordings are not routinely used in Finnish stroke units. In a systematic review by our study group, no plausible prescreening instrument for suggesting SDB in acute and subacute stroke patients exists (Takala, Puustinen, Rauhala, & Holm, 2018). Because of the limited resources, not all stroke patients can be tested for SDB, the prescreening tools for patients in need of sleep recordings can be valuable. According to ESOC guideline, SDB and particularly moderate to severe OSA is recommended to be treated with continuous positive airway pressure (CPAP; European Stroke Organisation (ESO) Executive Committee and ESO Writing Committee, 2008). Further, in the updated AHA/ASA guideline, it is proposed that the treatment with CPAP might be considered for improved outcomes for stroke and TIA patients (Kernan et al., 2014).

The aim of this observational longitudinal study is to focus on the relationships between SDB and clinical outcomes in Finnish stroke unit cohort. We aimed to evaluate the possible relationships between modified Rankin Scale (mRS) and severity of SDB and other outcome measures in first ever stroke and TIA patients. The participants were categorized to three classes of OSA according the respiratory recording in acute phase (non-OSA is AHI < 5/ hr, mild OSA is AHI 5-15/hr, and OSA is AHI > 15/hr). Central sleep apnea (CSA) was not included in the final analysis because it is known to be the consequence of stroke decreasing after acute phase (Parra et al., 2000). The assessed outcome measures are mRS in different time points (prehospital, registration day, hospital discharge, and follow-up of 12 months), duration of hospitalization, and need of rehabilitation. We hypothesized that patients with OSA have worse recovery causing higher need for rehabilitation and longer duration of hospitalization. If these patients can be recognized and tested earlier for OSA, faster initiation of CPAP is possible.

# 2 | MATERIAL AND METHODS

#### 2.1 | Study population

This study is a part of a larger research of sleep-disordered breathing in Finnish stroke patients in Satakunta Hospital District. Patients were recruited from the stroke unit between March 2013 and November 2016. We included 102 patients with first ever acute ischemic stroke or TIA who were able to give informed consent and had less than 72 hr from the hospital admission. Most patients had less than 72 hr of ischemic stroke or TIA symptom appearance. Few patients reported later that they had fluctuating symptoms or prior symptoms within the preceding week. Additionally, the patients were not allowed to have previous strokes, diagnosis, or treatment for sleep apnea. Moreover, the patients had to be conscious and not suffer from disabling aphasia to give written informed consent. The diagnosis of stroke or TIA was confirmed by Neurologist based on a history of a sudden onset of a neurologic deficit, clinical examination, and brain imaging. The registrations were conducted by Scientist during weekdays, from Monday to Thursday, due to practical reasons. Despite of that, patients admitted to stroke unit during weekend could be recruited and registered because of the inclusion criteria.

A detailed medical history and neurological examinations were done according to the hospital protocol by Neurologist. Following demographic data was collected by the Scientist: sex, age, smoking, previous diseases, marital status, education, and occupation. Body Mass Index (BMI) was calculated in all except three patients in non-OSA and OSA group and two in mild OSA group. BMI was categorized to BMI ≥ 30 and BMI < 30 and age-adjustment of BMI was made. The severity of the stroke was estimated by the National Institute of Health Stroke Scale (NIHSS; Brott et al., 1989) and disability was evaluated using Barthel Index scale (BI) on registration day (Mahoney & Barthel, 1965). Basic Nordic Sleep Questionnaires (BNSQ; Partinen & Gislason, 1995) were filled before registration. Computer tomography scan (CT) and on selected patients, magnetic resonance imaging (MRI) were performed. All routine laboratory tests, ECG and chest x-ray and blood pressure were examined according to the normal protocol of stroke and TIA patients.

This research project was approved by an Ethical board of Hospital District of Southwest Finland. Participation to the study was optional, and the participant had to give their written informed consent. The caregiver or relative could not give informed consent according to the Ethics committee.

# 2.2 | Assessment

Modified Rankin Scale (mRS) was assessed from full medical records and was made by Neurologist blinded by AHI severity. Disability was assessed with mRS before hospital admission, on registration day (mRSO), at hospital discharge (mRSexit), and follow-up of 12 months (mRSfollowup). We assessed mRS in each

patient in the different time points. The scale was divided to four categories: mRS 0, mRS 1-2, mRS 3-5, and mRS 6. The first category of mRS 0 includes patients who are asymptomatic and mRS 1-2 includes patients who have slight disability or any symptoms from stroke but are independent in Activity of Daily Living (ADL) functions. The two categories are defined as favorable outcome. Modified Rankin Scale 3-5 includes patients who have higher disability meaning the patient needs help at least in some ADL functions and mRS 6 is death and these two categories are defined as nonfavorable outcome. Duration of hospitalization was calculated from medical records and for analysis, it was divided to two groups, 2-4 days and 5-15 days. At the Neurologic ward, the present study is conducted, 4.3 days have been the average time spent in hospital. Thus, longer hospitalization (5-15 days) used in this study is over the average hospital stay. The information if patient needed rehabilitation was retrieved from medical records and rehabilitation included "basic" rehabilitation in rehabilitation units of health care centers and in multidisciplinary advanced rehabilitation units.

# 2.3 | Sleep study

All patients underwent overnight respiratory polygraphy on first or second night, within 48 hr, after admission to stroke unit. In this study, the recordings were made with NOX T3 wireless recorder (Copywright Nox Medical). The device measures ECG with a sampling frequency of 200 Hz, airflow with nasal cannulae, oxygen saturation with plethysmography, snoring sound, and breathing effort. Nocturnal respiratory recording measures respiratory events during sleep. It does not include EEG.

The recording devices were inserted in the afternoon for practical reasons, except the nasal cannulae which were placed before patient was going to sleep. The positioning of the nasal cannulae was done by the nurses. In the morning the Scientist helped the patient to take off the equipment and the data was later downloaded into the software for analysis. The analysis of the recordings was analyzed by Clinical Neurophysiologist.

The data was scored for apneas and hypopneas according to the recommendations of American Academy of Sleep Medicine (AASM 2012) and expressed as Apnea-Hypopnea Index (AHI; Berry et al., 2012). The definition of apnea is at least 90% drop of airflow signal lasting at least 10 s. Hypopnea is characterized by at least 30% drop in the airflow signal for 10 s or more. A contemporary drop of 3% or more in the blood oxygenation level should be present as well for it to count as hypopnea or arousal. If simultaneous pause in breathing effort measured by abdominal and thoracic belts occur, the apnea is classified as central. Apnea-Hypopnea Index (AHI) indicates the severity of apnea. It is represented in number of apneas or hypopneas per hour. Normal AHI is AHI < 5/hr whereas AHI ≥ 5/hr is considered as disordered. In this study, patients having AHI less than 5/hr as non-OSA and AHI 5 to 15/hr as mild OSA and AHI more than 15/hr which can be defined as moderate to severe OSA was classified

in this study as OSA. Patients with CSA were classified but not included in the final analyzes.

To measure breathing during sleep, the respiratory device records airflow using nasal cannulae that has two 1 cm long hoses that are placed to the nostrils. The nasal cannulae are attached to a pressure-sensitive transducer located in the respiratory device fixed on top of the patient's shirt. Two belts are used to detect physiological breathing efforts from thorax and abdomen. The efforts in belts produce changes in inductances of the coils wrapped inside the belts. The belts are attached to the same device as the nasal cannulae, so the respiratory efforts are registered to the transducer. Monitoring of respiratory events includes measuring the oxygen saturation (SaO2) with the finger probe pulse oximeter. In the modern devices, such as in NOX T3 used in the present study, the pulse oximeter has a wireless connection to the transducer that registers the oxygen saturation events.

#### 2.4 | Statistical analysis

Statistical analyses were performed using the SPSS software version 25.0. To compare stroke outcomes (mRS scale in four categories, hospitalization time, and need for rehabilitation both in two category) between OSA, mild OSA, and non-OSA groups, independent samples Kruskal–Wallis test was used. p value <.05 was considered as statistically significant result.

### 3 | RESULTS

Altogether, 102 patients with acute ischemic stroke or TIA referred to the stroke unit in our Hospital were included in the present study. Five patients were not analyzed due to technical problems or devices were detached. Two patients were excluded because of wrong diagnosis (intracerebral hemorrhage and glioma). The baseline characteristics of patients are illustrated in Table 1. Mean ages in each OSA group are quite similar. The proportion of males is 68% in both mild OSA and OSA patients compared to 42% of non-OSA patients. Mean BMI is higher in OSA group compared to non-OSA and mild OSA group. There are 19 patients (56%) in OSA group that are nonobese and after age-adjustment, 23 patients (68%) in OSA group have normal BMI. Patients with OSA have higher mean systolic blood pressure. There are same number of smokers in non-OSA and OSA patients but only one in mild OSA group. The frequencies of reported snoring retrieved from BNSQ in each group are quite similar. Barthel Index scale and NIHSS scores were assessed on the registration day and because of the inclusion criteria, the study consisted mainly mild strokes and TIA patients and that can be seen in high BI and low NIHSS scores on registration day. There are no differences in infarct locations in different OSA groups.

In total, 95 recordings were available for examination. A few patients with OSA had a combination of OSA and CSA and were classified to OSA group and four patients had pure CSA and they

**TABLE 1** Baseline characteristics of 91 patients

|   | non-OSA<br>n = 35 (38%) | mild OSA<br>n = 19 (21%) | OSA<br>n = 37 (41%) |
|---|-------------------------|--------------------------|---------------------|
|   | Min-Max (Mean)          | Min-Max (Mean)           | Min-Max (Mean)      |
| Age, years                                | 42-86 (61)              | 46-78 (63)               | 42-85 (67)          |
| Sex, male, <i>n</i> (%)                   | 15 (42%)                | 13 (68%)                 | 25 (68%)            |
| Body mass index, kg/m <sup>2</sup> (mean) | 18-40 (27)              | 22-32 (28)               | 23-41 (30)          |
| BMI < 30, n                               | 29                      | 13                       | 19                  |
| BMI ≥ 30, n                               | 3                       | 4                        | 15                  |
| BMI age-adjusted,<br>BMI < 30, n          | 29                      | 13                       | 23                  |
| Blood pressure, systolic mmHg             | 102-235 (153)           | 120-204 (157)            | 115-224 (70)        |
| Blood pressure, diastolic mmHg            | 54-111 (81)             | 63-116 (90)              | 51-136 (87)         |
| Smoking, yes, n (%)                       | 10 (29%)                | 1 (5%)                   | 10 (27%)            |
| Snoring (more than 1/<br>week) n (%)      | 20 (57%)                | 8 (42%)                  | 16 (43%)            |
| Barthel Index                             | 30-100 (93)             | 0-100 (94)               | 0-100 (81)          |
| NIHSS                                     | 0-8 (1.5)               | 0-7 (1.3)                | 0-18 (3)            |
| Hypertension arterialis, yes, n (%)       | 6 (45%)                 | 7 (37%)                  | 22 (59%)            |
| Diabetes mellitus, yes, n (%)             | 8 (22%)                 | 3 (19%)                  | 3 (8%)              |
| Location                                  |                         |                          |                     |
| Supratentorial, n (%)                     | 29 (83%)                | 15 (79%)                 | 30 (81%)            |
| Infratentorial, n                         | 6                       | 4                        | 7                   |

Note: BMI calculated in 32 of non-OSA, 17 of mild OSA, and 34 of OSA patients. Blood pressure, NIHSS and BI measured and assessed on registration day. Frequency of snoring reported in BNSQ questionnaire.

Abbreviations: BI, Barthel Index; BMI, Body Mass Index; NIHSS, National Institute of Health Stroke Scale; OSA, obstructive sleep apnea.

are not in included in following analyzes. According to registrations, there are 37% (n=35) non-OSA patients, 20% (n=19) of patients have mild OSA and 39% (n=37) have moderate/severe OSA (AHI > 15/hr) and 4% (n=4) have CSA (Figure 1). The prevalence of OSA defined as AHI > 15/hr is 39% and if mild OSA (AHI  $\geq 5$ /hr) is included, the frequency is 59%. Prehospital mRS was 0 (asymptomatic) in all except two patients who had mRS 2 because of musculoskeletal diseases. There were no deaths (mRS 6) in follow-up of 12 months.

Patients with OSA have higher proportion of disability scores of mRS 3–5 compared to non-OSA and mild OSA patients on registration day (mRSO, p=.009) and on hospital discharge (mRSexit p=.004). In non-OSA and OSA group there are almost same number of patients but in non-OSA group number of mRSO (asymptomatic) is high compared to OSA group. The number of higher disability score of mRS 3–5 in non-OSA patients on registration day is 4 (11%) and in OSA group 14 (38%) and, respectively on hospital discharge 3 (9%) in non-OSA group and 13 (35%) in OSA group (Figure 2). The differences are statistically significant on

registration day (p = .009) and on hospital discharge (p = .004). There was no statistical difference in disability among patients in follow-up of 12 months (mRSfollowup).

In OSA patients, the need of rehabilitation is increased (p=.039). Out of 91 patients, 25% patients (n=23) needed rehabilitation. Proportion of patients with OSA in rehabilitation unit is 65% (n=15) compared to non-OSA patients 17.5% (n=4) and mild OSA patients 17.5% (n=4). Proportion of non-OSA patients who needed rehabilitation is 11% (n=4). Proportion of mild OSA patients who needed rehabilitation is 21% (n=4) and patients with OSA who needed rehabilitation were 40% (n=15; Figure 3). The difference between non-OSA and OSA is statistically significant (p=.033).

Hospitalization time is longer in OSA patients (p=.045). In non-OSA patients, shorter duration of hospitalization (2–4 days) is found in 71% of patients and longer duration of hospitalization (5–15 days) in 29% of patients. In mild OSA patients, 53% patients had shorter duration of hospitalization and 47% longer duration. In OSA patients, 46% had shorter duration of hospitalization and 54% longer duration of hospitalization (Figure 4). The difference in hospitalization

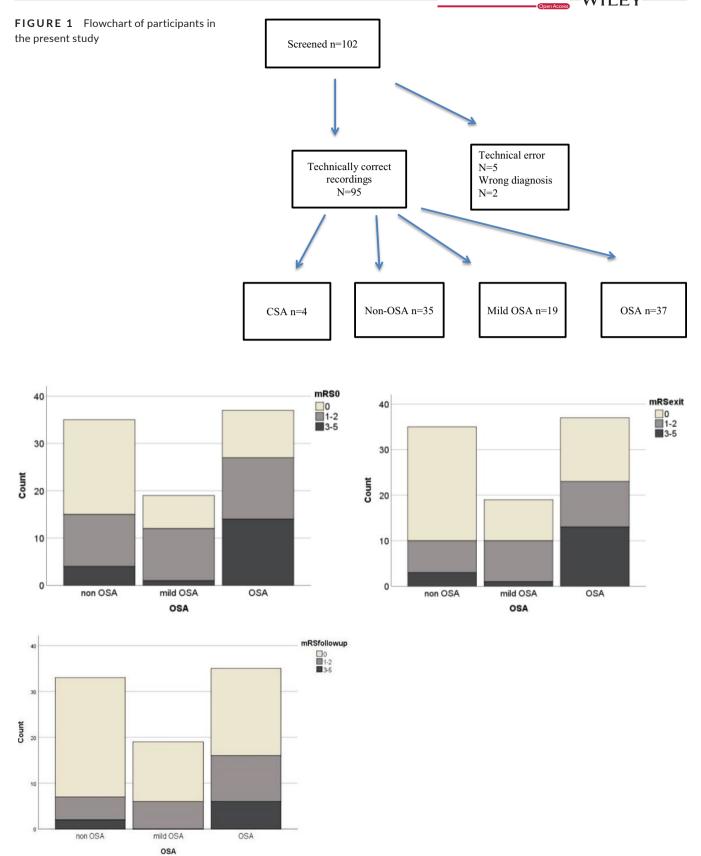
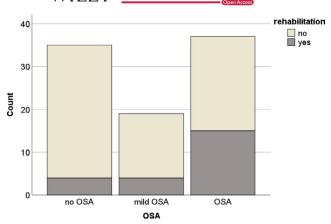


FIGURE 2 The numbers of non-OSA, mild OSA, and OSA patients in each mRS group in 3 follow-up points



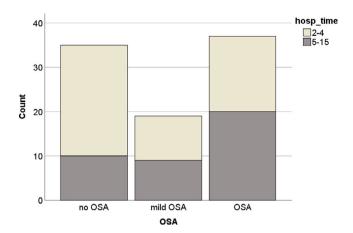
**FIGURE 3** Need of rehabilitation was higher in patients with OSA

length is statistically significant between OSA and non-OSA patients (p = .043).

#### 4 | DISCUSSION

The results in our study are comparable with previous studies, and we have some novel and interesting observations. The prevalence of OSA in the present study is 39% as defined by AHI > 15/hr and 59% as defined by AHI  $\geq$  5/hr and 4% of patients have CSA. The frequencies are similar to a Finnish study conducted by Väyrynen et al. (2014) with 42 mild ischemic stroke and TIA patients tested in stroke unit. Another Finnish study by Huhtakangas, Huhtakangas, Bloigu, and Saaresranta (2017) found high frequencies of OSA, over 85% (AHI  $\geq$  5/hr) in acute patients with and without thrombolysis. Johnson and Johnson (2010) made a meta-analysis of 29 studies with 2,343 ischemic or hemorrhagic stroke and TIA patients and the frequency of SDB was 72% (AHI > 5/hr) and 38% (AHI > 20/hr).

First, the important finding in this study is that the patients with OSA have higher proportion of nonfavorable disability scores compared to non-OSA and mild OSA patients on registration day and at hospital discharge. Despite our preliminary hypothesis, we could not show significant difference at disability at 12 months between the OSA groups. The results suggest that OSA could predispose as a risk factor with harmful consequences to more severe infarct and may affect stroke recovery during the first days. This finding is observed in our study even if there are mainly mild strokes. More than third, 38% of OSA patients have higher disability on registration day compared to 11% of non-OSA patients with higher disability. Further, on hospital discharge, still 35% of OSA patients have higher disability compared to only 9% of non-OSA patients. The differences are statistically significant. The same phenomenon has documented in previous studies. Kaneko et al. (2003) had a finding that patients with OSA have worse functional capacity measured with Functional Independence Measure score (FIM) at admission and at hospital discharge. The FIM is a more detailed assessment



**FIGURE 4** Duration of hospitalization (2–4 days or 5–15 days) in different OSA groups. The proportion of longer hospitalization (5–15 days) among OSA patients is seen 54% of patients compared to 29% of non-OSA patients. p = .045

tool than mRS scale used in our study. Menon, Sukumaran, Varma, and Radhakrishnan (2017) had a study similar to ours, and they observed worse short-term and long-term recovery among stroke patients with moderate to severe OSA compared to non-OSA patients measured with NIHSS and mRS scores. The results are comparable even if in our study NIHSS scores are lower in acute phase. Kim, Kim, Yang, Kim, and Kim (2015) found out that sleep disturbances screened with questionnaires were related to worse short and long-term outcome. Another study by the same group observed that sleep disturbances affect outcome even in patients with mild strokes (Kim et al., 2017).

Second, an interesting observation in our study is the high need of rehabilitation in patients with OSA. There are 40% of patients with OSA who needed rehabilitation compared to 11% of non-OSA patients. In mild OSA patients, the need of rehabilitation is 21%. The differences are statistically significant. Furthermore, we observed high proportion of patients with OSA in patients in need of rehabilitation (65%) compared to non-OSA patients (17.5%) and mild OSA patients (17.5%). In the study by Kaneko et al. (2003), prevalence of patients with OSA admitted to rehabilitation unit was 72% as defined by AHI over 10/hr.

With respect to our third outcome measure, duration of hospitalization, we found that almost half of the patients (54%) who have OSA in acute phase, had longer duration of hospitalization (5–15 days). In non-OSA patients, approximately, every fourth (29%) have longer hospitalization and the difference is statistically significant. Shorter hospital stay, 2–4 days is under the average hospitalization time in the neurologic ward this study was conducted. There are previous studies on the relationship between OSA and duration of hospitalization. In the study conducted by Kaneko et al. (2003), the main finding was that severity of OSA was correlated to both total length of hospitalization and to length of hospitalization in rehabilitation unit. Selic, M. Siccoli, Hermann, and Bassetti (2005) found an association between severity of OSA and duration of hospitalization in acute stroke patients.

We could not show difference in long-term outcome between the groups. We assume the reason for this is that in our stroke cohort we have mostly TIA and minor stroke patients, and the recovery is usually favorable in these patients. In addition, contrary to many studies, we conducted the registration in acute phase, during 72 hr after hospital admission. For example, in the guite similar study by Kaneko et al. (2003), the registration was done  $44.6 \pm 3.1$  days after hospital admission. Obstructive sleep apnea is known to improve after acute phase of stroke.

In our study we used AASM criteria for classifying severity of OSA, therefore the results can be compared with other similar studies. Further, the registrations in our study were done with more qualified portable wireless recorder with is approved by AASM guidelines (Berry et al., 2012). In addition, in our study the patients were registered in acute phase, during 72 hr of hospital admission. Even if we had mostly patients with minor strokes with low NIHSS and mRS scores and Finnish ischemic stroke cohort, the results are comparable with the study by Kim et al. (2015) with higher NIHSS scores and Asian cohort.

The potential limitations of our study can be the assessment of mRS scores retrospectively from medical records. In Finnish Health Care system, the medical records are electronic and accessible in most of regional Hospitals and in Health Care centers. The medical reports usually include information on the patients' ability to walk, possible support or help in ADL functions or use of social services for ADL or IADL functions. In addition, information on possible cognitive decline can be found in many medical records. We assessed NIHSS and BI score at registration day and decided to use mRS instead of BI as a follow-up measure. Modified Rankin Scale is more sensitive and useful outcome measure to show differences in mild strokes with minor neurologic deficits (Weimar et al., 2002). According to the inclusion criteria, mainly mild strokes and TIA patients could be included because no proxy was accepted to give informed consent. The patients with moderate or severe stroke who were co-operative and communicative could be recruited. In a cohort of more severe strokes, there could be more technical problems because of eventual poor co-operation during the registration.

Obstructive sleep apnea is known to precede the stroke unlike CSA that is a consequence of stroke (Bassetti & Aldrich, 1999; Bassetti et al., 1996; Parra et al., 2000). OSA is causing cerebral hypoxia by recurrent apneas and hypopneas and by reduced cardiac output (Bålfors & Franklin, 1994; Sahlin et al., 2008; Somers, 2008). Further, OSA is associated to increased platelet activation and increased fibrinogen but the mechanism is unknown (Ka"nel & Dimsdale, 2003). The proportion of higher disability among our study patients with OSA could be explained by the fact that OSA may aggravate stroke and impair recovery and that can also explain the high need of rehabilitation among these patients. The patients recruited to our study did not have a diagnosis of sleep apnea. In our study 39% of patients revealed to have moderate to severe OSA that should be treated with CPAP. OSA is underdiagnosed in women and nonobese persons and daytime sleepiness is not always present of unknown reasons in patients with heart failure (Arzt et al., 2006;

Bixler et al., 2001; Javaheri et al., 1998; Young et al., 2002). The same phenomenon is seen in stroke patients with sleep apnea as they do not report same amount of excessive sleepiness and have lower BMI values than sleep apnea patients without stroke (Arzt, Young, Finn, Skatrud, & Bradley, 2005). In our study, half of OSA (56%) patients are nonobese and if age-adjusted BMI is used, two thirds (68%) of OSA patients are normal weight meaning that even these patients might have SDB and they can have worse outcome. Our study suggests that the stroke patients with higher disability are more prone to have OSA, and they can be registered during acute phase. According to our study, there is no difference if the patients with higher disability are recognized and tested for OSA during the first days after admission or at hospital discharge. In addition, the stroke patients who need rehabilitation are also at a high risk of having OSA and could be tested. Several studies on early CPAP treatment in stroke patient with OSA have shown possible positive effects on stroke recovery and evolution and proven to be feasible with a compliance of 40%-60% (Bravata et al., 2011; Minnerup et al., 2012; Parra et al., 2011; Ryan, Bayley, Green, Murray, & Bradley, 2011).

# 5 | CONCLUSION

In conclusion, our observations in a Finnish stroke unit cohort are comparable with previous studies even in mainly mild stroke and TIA patients tested in acute phase. SDB and especially OSA is common in stroke and TIA patients. Sleep apnea has influences in many aspects of stroke care by causing higher disability and need for rehabilitation and can prolong hospitalization. OSA is not routinely screened among stroke patients even if it is a known risk factor. Because of limited resources in Finnish health care, not all stroke and TIA patients can be registered. Based on the findings in our study, prescreening tools for stroke patients suggesting for presence of OSA could be planned. In addition to patients with recognizable risk factors and symptoms for OSA, according to our study, it might be reasonable to evaluate the stroke patients with higher disability and the ones referred to rehabilitation unit. If the diagnosis of OSA can be made in stroke unit within first days after stroke onset, the initiation of CPAP treatment could be done during the hospitalization for possible better recovery.

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### **CONFLICT OF INTEREST**

None declared.

#### **AUTHOR CONTRIBUTION**

T-M.H.: contributed to design of the study, collecting data, analyzing and interpreting the results, and wrote most of the paper. J.P.: contributed to design of the study and participated in analyzing and interpreting the results. In addition, J.P. commented and provided revisions to scientific content of the manuscript. M.T.: contributed to design of the study and participated in collecting data, analyzing and interpreting the results. A.H.: contributed to design of the study and participated in analyzing and interpreting and writing part of the results. A.H. performed the statistical analysis of the paper. A.H commented and provided revisions to scientific content of the manuscript and given final approval.

#### PEER REVIEW

The peer review history for this article is available at https://publo ns.com/publon/10.1002/brb3.1762

#### DATA AVAILABILITY STATEMENT

Data available on request. Data includes sensitive data. Ethic committee statement for data usage is needed from the Ethics Committee of the Hospital District of Southwest Finland as well as permission to use data from Data register holder, Hospital District of Satakunta.

Ethics committee: http://www.vsshp.fi/en/tutkijoille/eetti nen-toimikunta/Pages/default.aspx

Data registry holder (in Finnish): https://www.satasairaala.fi/tutkimus/satakunnan-sairaanhoitopiirin-tutkimusluvat

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#### REFERENCES

- Arzt, M., Young, T., Finn, L., Skatrud, J. B., & Bradley, T. D. (2005). Association of sleep-disordered breathing and the occurrence of stroke. American Journal of Respiratory and Critical Care Medicine, 172, 1447–1451.https://doi.org/10.1164/rccm.200505-702OC
- Arzt, M., Young, T., Finn, L., Skatrud, J. B., Ryan, C. M., Newton, G. E., ... Bradley, T. D. (2006). Sleepiness and sleep in patients with both systolic heart failure and obstructive sleep apnea. Archives of Internal Medicine, 166, 1716–1722. https://doi.org/10.1001/archi.nte.166.16.1716
- Bålfors, E., & Franklin, K. (1994). Impairment of cerebral perfusion during obstructive sleep apneas. American Journal of Respiratory and Critical Care Medicine, 150, 1587–1591. https://doi.org/10.1164/ ajrccm.150.6.7952619
- Bassetti, C., & Aldrich, M. S. (1999). Sleep apnea in acute cerebrovascular diseases: Final report on 128 patients. Sleep, 22, 217–223. https:// doi.org/10.1093/sleep/22.2.217
- Bassetti, C., Aldrich, M. S., Chervin, R. D., & Quint, D. (1996). Sleep apnea in patients with transient ischemic attack and stroke: A prospective study of 59 patients. *Neurology*, 47, 1167–1173. https://doi. org/10.1212/WNL.47.5.1167
- Berry, R. B., Budhiraja, R., Gottlieb, D. J., Gozal, D., Iber, C., Kapur, V. K., ... Tangredi, M. M. (2012). Rules for scoring respiratory events in sleep: Update of the 2007 AASM manual for the scoring of sleep and associated events. *Journal of Clinical Sleep Medicine*, 08(05), 597–619. https://doi.org/10.5664/jcsm.2172
- Bixler, E. O., Vgontzas, A. N., Lin, H. M., Ten Have, T., Rein, J., Vela-Bueno, A., & Kales, A. (2001). Prevalence of sleep-disordered breathing in women: Effects of gender. American Journal of Respiratory and

- Critical Care Medicine, 163, 608-613. https://doi.org/10.1164/ajrccm.163.3.9911064
- Bravata, D. M., Concato, J., Fried, T., Ranjbar, N., Sadarangani, T., McClain, V., ... Yaggi, H. K. (2011). Continuous positive airway pressure: Evaluation of a novel therapy for patients with acute ischemic stroke. *Sleep*, *34*, 1271–1277. https://doi.org/10.5665/SLEEP.1254
- Brott, T., Adams, H. P., Olinger, C. P., Marler, J. R., Barsan, W. G., Biller, J., ... Hertzberg, V. (1989). Measurements of acute cerebral infarction: A clinical examination scale. *Stroke*, 20, 864–870. https://doi.org/10.1161/01.STR.20.7.864
- Collop, N. A., Anderson, W. M., Boehlecke, B., Claman, D., Goldberg, R., Gottlieb, D. J., ... Schwab, R. (2007). Clinical guidelines for the use of unattended portable monitors in the diagnosis of obstructive sleep apnea in adult patients. J Clin Sleep Med, 3(7), 737-747.
- Erkinjuntti, M., Salmi, T., Polo, O., & Kirjavainen, J. (2006). Suppea yöpolygrafia unenaikaisten hengityshäiriöiden diagnostiikassa. In *Kliininen neurofysiologia* (pp. 653-664). Helsinki, Finland: Duodecim.
- European Stroke Organisation (ESO) Executive Committee, ESO Writing Committee (2008) Guidelines for management of ischaemic stroke and transient ischaemic attack 2008. *Cerebrovascular Diseases*, 25, 457–507. https://doi.org/10.1159/000131083
- Good, D. C., Henkle, J. Q., Gelber, D., Welsh, J., & Verhulst, S. (1996).
  Sleep-disordered breathing and poor functional outcome after stroke.
  Stroke, 27, 252–259. https://doi.org/10.1161/01.STR.27.2.252
- Hermann, D. M., & Bassetti, C. L. (2009). Sleep-related breathing and sleep-wake disturbances in ischemic stroke. *Neurology*, 73, 1313– 1322. https://doi.org/10.1212/WNL.0b013e3181bd137c
- Hermann, D. M., & Bassetti, C. L. (2016). Role of sleep-disordered breathing and sleep-wake disturbances for stroke and stroke recovery. *Neurology*, 87, 1407–1416. https://doi.org/10.1212/WNL.00000 00000003037
- Huhtakangas, J. K., Huhtakangas, J., Bloigu, R., & Saaresranta, T. (2017).
  Prevalence of sleep apnea at the acute phase of ischemic stroke with or without thrombolysis. Sleep Medicine, 40, 40–46. https://doi.org/10.1016/j.sleep.2017.08.018
- Javaheri, S., Parker, T. J., Liming, J. D., Corbett, W. S., Nishiyama, H., Wexler, L., & Roselle, G. A. (1998). Sleep apnea in 81 ambulatory male patients with stable heart failure: Types and their prevalences, consequences, and presentations. *Circulation*, 97, 2154–2159. https:// doi.org/10.1161/01.CIR.97.21.2154
- Johnson, K. G., & Johnson, D. C. (2010). Frequency of sleep apnea in stroke and TIA patients: A meta-analysis. *Journal of Clinical Sleep Medicine*, 6, 131–137. https://doi.org/10.5664/jcsm.27760
- Kaneko, Y., Hajek, V. E., Zivanovic, V., Raboud, J., & Bradley, T. D. (2003).
  Relationship of sleep apnea to functional capacity and length of hospitalization following stroke. Sleep, 26, 293–297. https://doi.org/10.1093/sleep/26.3.293
- Kernan, W. N., Ovbiagele, B., Black, H. R., Bravata, D. M., Chimowitz, M. I., Ezekowitz, M. D., ... Wilson, J. A. (2014). Guidelines for the prevention of stroke in patients with stroke and transient ischemic attack: A guideline for healthcare professionals from the American heart association/American stroke association. Stroke, 45, 2160–2236. https://doi.org/10.1161/STR.000000000000024
- Kim, J., Kim, Y., Yang, K. I., Kim, D.-E., & Kim, S. A. (2015). The relationship between sleep disturbance and functional status in mild stroke patients. Annals of Rehabilitation Medicine, 39, 545–552. https://doi. org/10.5535/arm.2015.39.4.545
- Kim, K. T., Moon, H. J., Yang, J. G., Sohn, S. I., Hong, J. H., & Cho, Y. W. (2017). The prevalence and clinical significance of sleep disorders in acute ischemic stroke patients—A questionnaire study. Sleep and Breathing, 21, 759–765.https://doi.org/10.1007/s11325-016-1454-5
- Mahoney, F. I., & Barthel, D. W. (1965). Functional evaluation: The Barthel Index. Maryland State Medical Journal, 14, 61–65.



- Menon, D., Sukumaran, S., Varma, R., & Radhakrishnan, A. (2017). Impact of obstructive sleep apnea on neurological recovery after ischemic stroke: A prospective study. Acta Neurologica Scandinavica, 136, 419– 426. https://doi.org/10.1111/ane.12740
- Minnerup, J., Ritter, M. A., Wersching, H., Kemmling, A., Okegwo, A., Schmidt, A., ... Dziewas, R.. (2012). Continuous positive airway pressure ventilation for acute ischemic stroke: A randomized feasibility study. Stroke, 43, 1137–1139. https://doi.org/10.1161/STROK EAHA.111.637611
- Moyer, C. A., Sonnad, S. S., Garetz, S. L., Helman, J. I., & Chervin, R. D. (2001). Quality of life in obstructive sleep apnea: A systematic review of the literature. *Sleep Medicine*, 2, 477–491. https://doi.org/10.1016/S1389-9457(01)00072-7
- Parra, O. L., Arboix, A., Bechich, S., Garcia-Eroles, L. U., Montserrat, J. M., Lopez, J. A., ... Sopena, J. J. (2000). Time course of sleep-related breathing disorders in first-ever stroke or transient ischemic attack. American Journal of Respiratory and Critical Care Medicine, 161, 375–380. https://doi.org/10.1164/ajrccm.161.2.9903139
- Parra, O., Arboix, A., Montserrat, J. M., Quinto, L., Bechich, S., & Garcia-Eroles, L. (2004). Sleep-related breathing disorders: Impact on mortality of cerebrovascular disease. *European Respiratory Journal*, 24, 267–272. https://doi.org/10.1183/09031936.04.00061503
- Parra, O., Garcia-Esclasans, N., Montserrat, J. M., Eroles, L. G., Ruiz, J., López, J. A., ... Sopena, J. J. (1997). Should patients with sleep apnoea/hypopnoea syndrome be diagnosed and managed on the basis of home sleep studies? *European Respiratory Journal*, 10, 1720–1724.
- Parra, O., Sánchez-Armengol, A., Bonnin, M., Arboix, A., Campos-Rodríguez, F., Pérez-Ronchel, J., ... Jiménez, M. C. (2011). Early treatment of obstructive apnoea and stroke outcome: A randomised controlled trial. *European Respiratory Journal*, 37, 1128–1136.https://doi.org/10.1183/09031936.00034410
- Partinen, M., & Gislason, T. (1995). Basic Nordic Sleep Questionnaire (BNSQ): A quantitated measure of subjective sleep complaints. *Journal of Sleep Research*, 4, 150–155. https://doi.org/10.1111/j.1365-2869.1995.tb00205.x
- Ryan, C. M., Bayley, M., Green, R., Murray, B. J., & Bradley, T. D. (2011). Influence of continuous positive airway pressure on outcomes of rehabilitation in stroke patients with obstructive sleep apnea. *Stroke*, 42, 1062–1067. https://doi.org/10.1161/STROKEAHA.110.597468
- Sahlin, C., Sandberg, O., Gustafson, Y., Bucht, G., Carlberg, B., Stenlund, H., & Franklin, K. A. (2008). Obstructive sleep apnea is a risk factor for death in patients with stroke: A 10-year follow-up. Archives of Internal Medicine, 168, 297. https://doi.org/10.1001/archinternmed.2007.70
- Selic, C., M. Siccoli, M., Hermann, D. M., & Bassetti, C. L. (2005). Blood pressure evolution after acute ischemic stroke in patients with and without sleep apnea. Stroke, 36, 2614–2618. https://doi. org/10.1161/01.STR.0000189689.65734.a3

- Somers, V. K., White, D. P., Amin, R., Abraham, W. T., Costa, F., Culebras, A., Daniels, S., ... Young, T. (2008). Sleep apnea and cardiovascular disease: an American Heart Association/American College of Cardiology Foundation Scientific Statement from the American Heart Association Council for High Blood Pressure Research Professional Education Committee, Council on Clinical Cardiology, Stroke Council, and Council on Cardiovascular Nursing. Journal of the American College of Cardiology, 52(8), 686-717. https://doi.org/10.1016/j.jacc.2008.05.002
- Somers, V. K., Dyken, M. E., Clary, M. P., & Abboud, F. M. (1995) Sympathetic neural mechanisms in obstructive sleep apnea. The Journal of Clinical Investigation, 96, 1897-1904. https://doi. org/10.1172/JCI118235
- Takala, M., Puustinen, J., Rauhala, E., & Holm, A. (2018). Pre-screening of sleep-disordered breathing after stroke: A systematic review. *Brain and Behavior*, 8(12), e01146. https://doi.org/10.1002/brb3.1146
- Urbano, F., Roux, F., Schindler, J., & Mohsenin, V. (2008). Impaired cerebral autoregulation in obstructive sleep apnea. *Journal of Applied Physiology*, 105, 1852–1857. https://doi.org/10.1152/japplphysiol.90900.2008
- Väyrynen, K., Kortelainen, K., Numminen, H., Miettinen, K., Keso, A., Tenhunen, M., ... Himanen, S. L. (2014). Screening sleep disordered breathing in stroke unit. Sleep Disorder, 2014, 1–7. https://doi. org/10.1155/2014/317615
- von Ka"nel, R., & Dimsdale, J. E. (2003). Hemostatic alterations in patients with obstructive sleep apnea and the implications for cardiovascular disease. *Chest*, 124, 1956–1967. https://doi.org/10.1378/chest.124.5.1956
- Weimar, C., Kurth, T., Kraywinkel, K., Wagner, M., Busse, O., Haberl, R. L., & Diener, H.-C. (2002). Assessment of functioning and disability after ischemic stroke. *Stroke*, 33, 2053–2059. https://doi.org/10.1161/01. STR.0000022808.21776.BF
- Yaggi, H. K., Concato, J., Kernan, W. N., Lichtman, J. H., Brass, L. M., & Mohsenin, V. (2005). Obstructive sleep apnea as a risk factor for stroke and death. New England Journal of Medicine, 353, 2034–2041. https://doi.org/10.1056/NEJMoa043104
- Young, T., Peppard, P. E., & Gottlieb, D. J. (2002). Epidemiology of obstructive sleep apnea: A population health perspective. American Journal of Respiratory and Critical Care Medicine, 165, 1217–1239. https://doi.org/10.1164/rccm.2109080

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