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OSA Treatment Lowers the Risk of Declining Daily Activities

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ABSTRACT:

Background: The aim of the study was to investigate whether severe obstructive sleep apnea (OSA) had association with quality of life (QOL), fatigue and functional ability seven years after ischemic stroke.
Methods: A total of 204 ischemic stroke patients were included in the study during 2013-2015. After seven years the 136 survivors had a structured interview by telephone focusing on subjective QOL, functional ability, fatigue, depression, and insomnia.
Results: Of alive patients, 136/99.3% answered the questionnaires. The mean age was 64.2 years, 41.9 % were men, and 54/40% had respiratory event index (REI) ≥30/h. Those with REI ≥ 30 were more obese (29.2% vs 26.6%, $p < 0.001$), and coronary artery disease (25.9% vs 12.2%, $p = 0.04$), had lower Barthel Index (BI) (88.3 vs 92.3, $p = 0.014$), higher modified Rankin Scale (mRS) (2 vs 1, $p = 0.025$), and more need of medical aids (18.4 vs 13.2, $p = 0.004$). The QOL was good, but lower (6.98 vs 6.48, $p = 0.056$) and mobility domain was significantly worse (1.5 vs 1.3, $p = 0.019$) among severe OSA (REI) ≥30/h) patients. The CPAP treatment associated with an impaired risk of decreased usual activities (OR 0.190, 95% CI 0.042-0.857, $p = 0.031$). Though severe OSA was not an independent risk factor for functional ability, whereas higher BMI was an independent risk factor for impaired QOL ($p = 0.006$, 95%CI 1.047-1.315).
Conclusions: Seven years post-stroke the QOL was in good level, although it tended to be lower in stroke patients with severe OSA. The CPAP treatment associated with better usual activities in patients with severe OSA.

1. Introduction

Sleep apnea prevalence among stroke patients varies between 62.5 and 91.2 % [1,2]. Stroke patients have four- to six-fold risk for obstructive sleep apnea (OSA) [3]. Ischemic stroke patients with OSA tend to have poor neurological and functional recovery and higher mortality risk [4,5]. OSA is an independent risk factor for stroke [6]. One previous study pointed out, that sleep-disordered breathing was associated with worse functional outcome, but not neurologic or quality of life (QOL) outcomes three months post-stroke [7].

Former studies showed that psychosocial and physical factors are important predictors for QOL after stroke [8]. Advancing age, smoking, diabetes, atrial fibrillation, and stroke subtype may have association with poor functional outcome after stroke [4]. According to a long-term post-stroke evaluation mobility status decline in every fifth of stroke patients. Predictors of mobility decline are inactivity, fatigue and depression [9].

OSA itself has a negative impact on QOL [10]. According to literature, untreated OSA has a negative impact on recovery of stroke, recurrent ischemic stroke, and higher long-term mortality [4,11,12], although not confirmed in all studies [13]. Continuous Positive Airway Pressure (CPAP) treatment after stroke may lead to faster functional recovery and improved QOL [14,15].

Up to 37% of stroke survivors experience insomnia with daytime

Abbreviations: OSA, Obstructive Sleep Apnea; QOL, Quality of life; REI, Respiratory event index; BI, Barthel Index (BI); mRS, Modified Rankin Scale; CPAP, Continuous Positive Airway Pressure; ESS, Epworth Sleepiness Scale; GCS, Glasgow Coma Scale; NIHSS, National Institutes of Health Stroke Scale; EQ-5D, European Quality of Life-5 Dimensions; FSS-9, Fatigue Severity Scale; ISI, Insomnia Severity Index; ADL, Activities of daily living; OR, odds ratio.

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consequences and poststroke insomnia is associated with depression, disability and fatigue [16,17]. According to the literature independent outcomes of post-stroke depression are higher mortality after ten years, decreased QOL and disability after one year [18,19]. Post-stroke fatigue is common, and it associates with older age, higher modified Rankin Scale (mRS) scores, depressive symptoms, hypercholesterolemia, and decreased QOL in ischemic stroke patients [20].

There are only a few studies which have evaluated long-term association between OSA and post-stroke QOL and functional recovery [3,4] In this study we evaluated the impact of OSA on QOL, functional activity, fatigue, insomnia, and depression after stroke.

2. Participants and methods

2.1. Participants and data collection

We performed an observational, single center study in 204 ischemic stroke patients aged 18 years or over admitted to the Stroke Unit at the Department of Neurology of the Oulu University Hospital from April 2013 to January 2015. Participation was voluntary and non-cooperative patients excluded. We obtained written informed consent from all patients or from their caregivers. The ethics committee of the Northern Ostrobothnia Hospital District approved the study protocol.

The patients were followed prospectively until 2021. The same investigator made a structured telephone-interview during April and November 2021 to all study patients. If the patient was unable to answer the questions, caregivers answered them. Only one patient denied attending the study. The flowchart of study patients is shown in Fig. 1.

The baseline demographic data included age, gender, body mass index, current smoking habits, daily alcohol consumption, comorbidities, vascular risk factors and stroke location. Stroke outcome was estimated by mRS (scale 0–5) [21], while Barthel Index (BI) (scale 0–100) was documented only after follow-up [22]. We assessed the level of consciousness by the Glasgow Coma Scale (GCS; scale 3–15) [23], and stroke severity by the National Institutes of Health Stroke Scale (NIHSS, scale 0–35) [24].

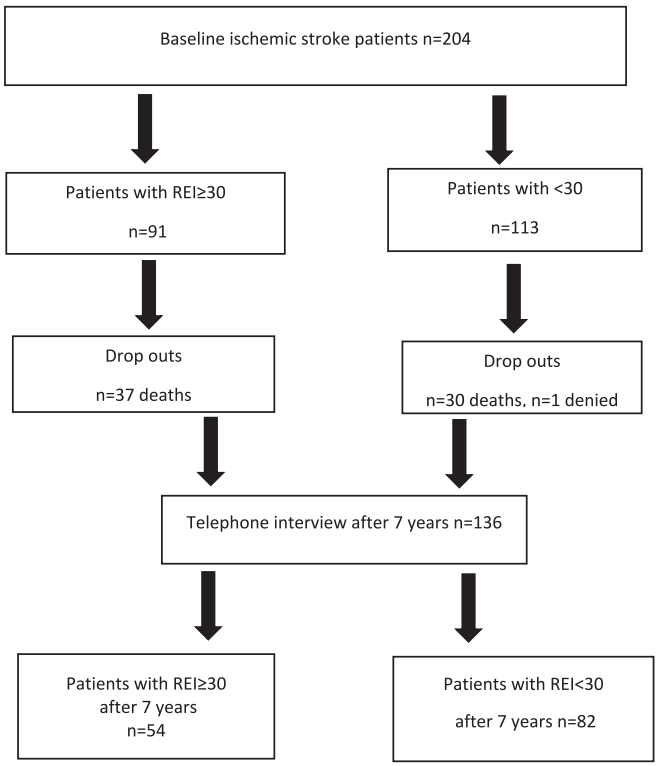

Fig. 1. Flow Chart of participant selection.

The telephone interview and specific questionnaire included questions on functional ability (BI, mRS) [21,22], health-related QOL questionnaire: European Quality of Life-5 Dimensions (EQ-5D) [25], fatigue questionnaire: Fatigue Severity Scale (FSS-9) [26], sleep questionnaire: Insomnia Severity Index (ISI) [27], Epworth Sleepiness Scale (ESS) [28]. We also made questions about smoking habits, employment status (retired or employed), living condition, disabilities and need of caregiver or medical aids (wheelchair, wheel walker, walking stick). We collected the data of diagnosis of depression and death from medical records. The comorbidities were updated.

Activities of daily living (ADL) was measured by BI, which included 10 items of ADL; feeding, bathing, grooming, dressing, bowel and bladder care, toilet use, transfer to bed and chair, mobility and stair climbing. The BI scores 100 indicated full ability and score 0 showed full disability. The BI has been reported to be a reliable and validated measure of ADL in stroke patients [29]. We used mRS to assess the dependence and score 0 indicated full independence and 5 full dependence [21].

The study patients self-rated their QOL by answering the European quality of life-questionnaire (EQ-5D), which has been applied and validated for stroke patients [25,30]. At follow-up the respondents described their own health state on five dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Based on the EQ-5D scores QOL is good (5 points), moderate (10 points) or reduced (15 points). We used the modified standard five-dimensional format with three levels: no problems, some problems, or extreme problems.

Fatigue after stroke was assessed by the fatigue severity scale (FSS-9) only after follow-up [26]. The FSS-9 contained nine questions and the patients rated each question by choosing appropriate number between 0 and 7. At first the total scores vary from 9 to 63 and then the score is divided by the number of responded questions and in the end the total scores range from 1 to 7. The FSS-9 points $\geq$ 4 means that the patient experiences fatigue [31].

We used Epworth Sleepiness Scale (ESS; scale 0–24) to assess daytime sleepiness and ESS $\geq$ 10 indicating excessive daytime sleepiness [28]. The Insomnia Severity Index (ISI, scale 0–28) scores $\geq$8 indicated that the patient has insomnia [27].

2.2. Cardiorespiratory polygraphy

An unattended cardiorespiratory polygraphy with a 3-channel portable device (ApneaLinkPlus, Resmed, Sydney, Australia) was performed on study patients in acute phase as described previously [1]. Sleep apnea was defined as a respiratory event index (REI) greater than or equal to 5/h and severe sleep apnea was determined as an REI greater than or equal to 30/h. Moderate sleep apnea was specified as REI 16–29/h and mild sleep apnea determined as REI 5–15/h. We divided the study group as follows: patients with REI $\geq$ 30 were in severe OSA group and REI $<$ 30 included patients with moderate and mild sleep apnea or those without sleep apnea.

2.3. Statistical analysis

Patients` demographic data was reported as means and standard deviations (SD) or as frequencies and percents. The mRS, the NIHSS and GCS scores were reported as medians. The variables measured at baseline were compared between the groups with and without severe sleep apnea using the Chi-square test or the Fisher's exact test (categorical variables), the Student's *t*-test (normally distributed variables), or the Mann-Whitney *U* test (skewed distributions), separately for all the patients included at baseline and in the follow-up data. Logistic regression analyses were performed to evaluate odds ratios (OR) and 95% confidence intervals (CI) of variables that predict QOL after stroke. The *p* value of $<$0.05 was considered statistically significant. Statistical analyses were performed using IBM SPSS (IBM Corp. Released 2013. IBM

SPSS Statistics for Windows, Version 29.0.1.0 Armonk, NY: IBM Corp.).

3. Results

The patients` baseline characteristics and clinical data at admission and after seven years in alive patients are shown in Table 1. Of all patients at admission, 62.7% were male, and the gender distribution did not differ between the two groups. Of the 204 patients, 137 (67.2%) survived, of whom 136 (99.3%) agreed to participate in the telephone interview seven years post-stroke and those 136 patients (66.7%) (Fig. 1.) were included in the final analyses. The mean time from stroke onset to the telephone interview was 7.5 years, range 6.3–8.7 years. At baseline, severe OSA was present in 39.7%, moderate OSA in 25.0%, mild OSA in 25.7% and 9.6% did not have sleep apnea. The patients having severe OSA were older than other patients at admission (mean age difference 4.6 years; $p = 0.017$) and had more often coronary artery disease, higher median prestroke Rankin Scale and median NIHSS score but there was no difference between groups after seven years. The mean BMI was higher in the severe OSA group as compared to the others. After seven years the patients having severe OSA had more often hypertension than others. There were no between-group differences concerning smoking prevalence, daily alcohol consumption, daytime sleepiness, diagnosed depression, hypercholesterolemia, diabetes mellitus, heart failure, aphasia, atrial fibrillation, the location of infarction, or peripheral arterial disease at follow-up either.

The functional outcomes and QOL seven years after the ischemic stroke are presented in Table 2. The overall mean BI was 90.74, and it was worse in the severe OSA group 88.33 vs. 92.32 ($p = 0.014$). The overall median mRS was 1.00, and it was elevated in the severe OSA group compared to the others 2.00 vs 1.00 ($p = 0.025$). The mean EQ-5D was 6.68 and did not differ statistically between the groups (6.98 vs 6.48, $p = 0.056$). The patients with severe OSA had impaired mean mobility compared to the others 1.52 vs. 1.32 ($p = 0.019$), but there was no difference in mean usual activities (1.37 vs. 1.41), self-care (1.39 vs. 1.27), pain or discomfort (1.43 vs. 1.39) or anxiety or depression (1.17 vs. 1.21) between the groups. Fatigue was reported less frequently in severe OSA group 29.2% vs. 34.1% but the difference was nonsignificant. There was no difference in the mean FSS-9 between the groups. The mean ESS was higher in severe OSA group 4.35 vs. 3.72 but the difference was not significant ($p = 0.169$). There was no difference in terms of being at work after seven years. Those who had severe OSA needed care more frequently than others 40.7% vs. 25.6% but the difference was not significant ($p = 0.063$). The need of medical aids was higher among those with severe OSA compared to the others 46.3% vs. 22.0% ($p = 0.003$) but the need of institutional care was equal 11.1% vs 8.5%. There was no difference in the mean insomnia severity index between the groups. The amount of insomnia (25.9% vs. 30.5%) and depression (16.7% vs. 19.5%) was statistically equal though they both

Table 1
The baseline characteristics and clinical data at admission and seven years after stroke.

Characteristic	At admission				After seven years			
	Subjects with REI ≥ 30 ($n = 91$)	Subjects with REI < 30 ($n = 113$)	Total ($n = 204$)	*P*-value	Subjects with REI ≥ 30 ($n = 54$)	Subjects with REI < 30 ($n = 82$)	Total ($n = 136$)	P-value
Men,n (%)	58 (63.7)	70 (61.9)	128 (62.7)	0.793	33 (38.9)	46 (43.9)	79 (41.9)	0.562
Mean Age, years (SD)	70.3 (12.5)	65.7 (13.8)	67.7 (13,4)	**0.017**	66.5 (11.7)	62.6 (13.3)	64.2 (12.8)	0.101
Mean BMI (SD)	28.2 (4.7)	26.5 (4.6)	27.3 (4.7)	**0.005**	29.2 (4.2)	26.6 (4.1)	27.6 (4.3)	**<0.001**
Smoking n (%)	21 (23.1)	23 (20.4)	44 (21.6)	0.638	7 (13)	9 (11)	16 (11.8)	0.725
Alcohol consumption daily n (%)	4 (4.4)	4 (2.7)	7 (3.4)	0.702	2 (3.7)	3 (3.7)	5 (3.7)	1.000
Mean ESS (SD)	5.0 (2.8)	4.4 (2.9)	4.7 (2.8)	0.179	4.4 (2.7)	3.7 (3.1)	4.7 (2.9)	0.223
Median prestroke Rankin Scale (SD)	0 (1.2)	0 (1.1)	0 (1.2)	**0.049**	0 (0.8)	0 (0.9)	0 (0.8)	0.367
Median NIHSS score (SD) (0–35)	5.0 (5.5)	3.0 (4.2)	4.0 (4.9)	**0.005**	4 (4.9)	3 (4.0)	4.9 (4.4)	0.067
Aphasia n (%)	26 (28.6)	20 (17.7)	46 (22.5)	0.065	9 (16.7)	15 (18.3)	24 (17.6)	0.808
Median GCS score (SD) (3–15)	15.0 (1.6)	15.0 (1.0)	15.0 (1.3)	0.096	15.0 (0.9)	15.0 (1.0)	15.0 (1.0)	0.682
Hypertension n (%)	61 (67.0)	62 (54.9)	123 (60.3)	0.078	37 (68.5)	38 (46.3)	75 (55.1)	**0.011**
Hypercholesterolemia n (%)	46 (50.5)	47 (41.6)	93 (45.6)	0.202	23 (42.6)	31 (37.8)	54 (39.7)	0.577
Diabetes Mellitus n (%)	23 (25.3)	17 (15.0)	40 (19.6)	0.067	10 (18.5)	8 (9.8)	18 (13.2)	0.140
Coronary Artery Disease n (%)	29 (31.9)	20 (17.7)	49 (24.0)	**0.019**	14 (25.9)	10 (12.2)	24 (17.6)	**0.040**
Heart Failure n (%)	6 (6.6)	4 (3.5)	10 (4.9)	0.346	1 (1.9)	3 (3.7)	4 (2.9)	1.000
Atrial Fibrillation n (%)	18 (19.8)	14 (12.4)	32 (15.7)	0.149	8 (14.8)	4 (4.9)	12 (8.8)	0.063
PAD n (%)	5 (5.5)	2 (1.8)	7 (3.4)	0.246	3 (5.6)	1 (1.2)	4 (2.9)	0.301
Mean ISI (SD)	3.44 (3.3)	4.3 (3.9)		0.201	5.74 (4.1)	5.9 (4.1)		0.835
Insomnia n (%)	3 (2.2)	10 (7.4)	13 (9.6)	0.225	14 (10.3)	25 (18.4)	39 (28.7)	0.699
Depression n (%)	0 (0)	3 (2.7)	3 (1.5)	0.255	9 (16.7)	16 (19.5)	25 (18.4)	0.675
Stroke Location: Middle cerebral artery infarction n (%)	45 (49.5)	53 (46.9)	98 (48.0)	0.717	21 (38.9)	39 (47.6)	60 (44.1)	0.319
Stroke Location: Lacunar infarction n (%)	27 (29.7)	26 (23.0)	53 (26.0)	0.281	20 (37.0)	18 (22.0)	38 (27.9)	0.055
Retired n (%)					47 (87)	67 (81.7%)	114 (83.8)	0.409

BMI, body mass index; ESS, Epworth Sleepiness Scale; NIHSS, National Institutes of Health Stroke Scale; GCS, Glasgow Coma Scale; PAD, peripheral arterial disease; ISI, insomnia Severity Index.

Table 2
Functional outcomes and quality of life after seven years.

Outcome	Patients with REI ≥ 30 (n = 54)	Patients with REI < 30 (n = 82)	Total (n = 136)	P
Mean Barthel Index (SD)	88.33 (18.81)	92.32 (20.14)	90.74 (19.65)	**0.014**
Median mRS (SD)	2.00 (1.61)	1.00 (1.43)	1.00 (1.53)	**0.025**
Mean EQ-5D (SD)	6.98 (1.89)	6.48 (1.88)	6.68 (1.89)	0.056
Mean Usual activities EQ-5D (SD)	1.37 (0.61)	1.41 (0.65)	1.39 (0.62)	0.070
Mean Mobility EQ-5D (SD)	1.52 (0.54)	1.32 (0.52)	1.40 (0.53)	**0.019**
Mean Self-care EQ-5D (SD)	1.39 (0.63)	1.27 (0.57)	1.32 (0.59)	0.085
Mean Pain or discomfort EQ-5D (SD)	1.43 (0.54)	1.39 (0.52)	1.40 (0.52)	0.503
Mean Anxiety or depression EQ-5D	1.17 (0.38)	1.21 (0.41)	1.19 (0.40)	0.235
Fatigue n (%)	16 (29.6)	28 (34.1)	44 (32.4)	0.582
Mean FSS-9 (SD)	24.06 (15.10)	24.78 (17.16)	24.49 (16.32)	0.885
Mean ESS (SD)	4.35 (2.72)	3.72 (3.08)	3.97 (2.95)	0.169
Retired n (%)	47 (87.0)	67(81.7)	114 (83.8)	0.409
Need of care n (%)	22 (40.7)	21 (25.6)	43 (31.6)	0.063
Medical aids n (%)	25(46.3)	18 (22.0)	43 (31.6)	**0.003**
Institutional care n (%)	6 (11.1)	7 (8.5)	13 (9.6)	0.617
Mean Insomnia Severity Index (SD)	5.74 (4.13)	5.89 (4.05)	5.83 (4.07)	0.673
Insomnia n (%)	14 (25.9)	25 (30.5)	39 (28.7)	0.565
Depression n (%)	9 (16.7)	16 (19.5)	25 (18.4)	0.675

mRS, Modified Rankin Scale; EQ-5D, European Quality of life-5 Dimensions; FSS-9, Fatigue Severity Scale; ESS, Epworth Sleepiness Scale; REI, Respiratory event index.

tend to be rarer in the severe OSA group.

The exact data for normal BI and EQ-5D after 7 years of follow-up are presented in the Table 3. In the severe OSA group 30 (55.6%) had normal BI and 14 (25.9%) had normal EQ-5D while in others the corresponding numbers were 63 (76.8%) and 34 (41.5%). There were significantly less patients having normal BI in the severe OSA group ($p = 0.009$). Those without severe OSA had less often problems with walking than patients who had severe OSA ($p = 0.015$). Patients with severe OSA had more problems with self-care and usual activities than others (31.5% vs. 20.7% and 40.8% vs. 25.6%) but the differences were not significant. There were 22 (40.8%) patients suffering pain or discomfort in the severe OSA group and 31 (37.8%) in others. In the severe OSA group there were 9 (16.7%) anxious or depressed patients and 17 (20.7%) among others. None of the patients were extremely anxious or depressed.

The univariate logistic regression analysis for the influence of the severity of the stroke (NIHSS) and severe OSA on the QOL are presented in Table 4. We found out that severe OSA is associated with the risks of decreased BI (OR 2.37, 95% CI 1.09–5.14), need of mobility aid (OR 2.95, 95% CI 1.39–6.29), and decreased mobility (OR 2.30, 95% CI 1.12–4.75). On the other hand, the severity of the stroke is associated with the risks of decreased BI (OR 1.15 95% CI 1.05–1.26), need of care (OR 1.14, 95% CI 1.05–1.25), decreased selfcare (OR 1.12, 95% CI 1.03–1.22), and decreased usual activities (OR 1.15, 95% CI 1.05–1.26).

After multivariable logistic regression we found that the elevated BMI predicted lower EQ-5D (OR 1.174, $p = 0.006$, 95% CI 1.047–1.315) and worse pain EQ-5D (OR 1.126, $p = 0.011$, 95% CI 1.028–1.233) independently. Independent risk factors for impaired mobility EQ-5D were elevated BMI (OR 1.130, $p = 0.032$, 95% CI 1.010–1.263), impaired admission mRS (OR 2.264, p = 0.011, 95% CI 1.205–4.253) and age (OR 1.100, $p < 0.001$, 95% CI 1.052–1.172). Impaired admission mRS (OR 2.261, $p = 0.007$,95% CI 1.247–4.099), elevated NIHSS (OR 1.188, $p = 0.004$, 95% CI 1.057–1.336) and age (OR 1.125, $p < 0.001$, 95% CI 1.055–1.199) predicted independently impaired self-care EQ-5D, impaired performance in daily activities EQ-5D (OR 2.408, p =

Table 3
EQ-5D and normal Barthel Index after seven years of follow-up.

	Patients with REI ≥ 30 (n = 54)	Patients with REI < 30 (n = 82)	Total (n = 136)	P
Normal EQ-5D (%)	14 (25.9)	34 (41.5)	48 (35.3)	0.064
Mobility Domain				
No problems with walking (%)	27(50.0)	58(70.7)	85 (62.5)	**0.015**
Some problems with walking (%)	26(48.1)	22(26.8)	48 (35.3)	**0.011**
Confined to bed (%)	1(1.9)	2(2.4)	3(2.2)	1.000
Self-care Domain				
No problems with self-care (%)	37(68.5)	65(79.3)	102 (75.0)	0.157
Some problems with washing or dressing (%)	13(24.1)	12(14.6)	25 (18.4)	0.164
Unable to wash or dress (%)	4(7.4)	5(6.1)	9(6.6)	0.741
Usual activities Domain				
No problems with usual activities (%)	32(59.3)	61(74.4)	93 (68.4)	0.063
Some problems with usual activities (%)	17(31.5)	16(19.5)	33 (24.3)	0.111
Unable to do usual activities (%)	5(9.3)	5(6.1)	10(7.4)	0.518
Pain or discomfort Domain				
No pain or discomfort (%)	32(59.3)	51(62.2)	83 (61.0)	0.731
Moderate pain or discomfort (%)	21(38.9)	30(36.6)	51 (37.5)	0.786
Extreme pain or discomfort (%)	1(1.9)	1(1.2)	2(1.5)	1.000
Anxiety or depression Domain				
Not anxious or depressed (%)	45 (83.3)	65 (79.3)	110 (80.9)	0.555
Moderately anxious or depressed (%)	9(16.7)	17(20.7)	26 (19.1)	0.555
Extremely anxious or depressed (%)	0	0	0	
Normal Barthel index (score = 100) (%)	30 (55.6)	63 (76.8)	93 (68.4)	**0.009**

EQ-5D, European Quality of Life-5 Dimensions; REI, Respiratory event index.

Table 4
The effect of the severity of stroke and severe OSA on the quality of life after an ischemic stroke after seven years of follow-up.

	NIHSS (severity of stroke)			Severe OSA (REI ≥ 30)		
	OR	95% CI	P-value	OR	95% CI	P-value
Barthel <100	**1.15**	**1.05–1.26**	**0.002**	**2.37**	**1.09–5.14**	**0.029**
Need of institutional care	1.04	0.92–1.17	0.511	1.26	0.39–4.05	0.696
Need of care	**1.14**	**1.05–1.25**	**0.003**	1.74	0.81–3.76	0.156
Need of mobility aid	1.03	0.95–1.12	0.492	**2.95**	**1.39–6.29**	**0.005**
Decreased EQ-5D	1.06	0.96–1.16	0.241	1.90	0.89–4.07	0.097
Fatigue	1.05	0.97–1.14	0.207	0.75	0.35–1.60	0.460
Insomnia	0.98	0.90–1.07	0.692	0.82	0.38–1.78	0.611
Decreased mobility	1.04	0.96–1.13	0.347	**2.30**	**1.12–4.75**	**0.024**
Decreased selfcare	**1.12**	**1.03–1.22**	**0.012**	1.53	0.68–3.45	0.303
Decreased usual activities	**1.15**	**1.05–1.26**	**0.002**	1.74	0.81–3.76	0.158
Pain	0.99	0.91–1.07	0.772	1.15	0.56–2.34	0.701
Anxiety or depression	1.03	0.94–1.14	0.513	0.73	0.30–1.81	0.496

EQ-5D, European Quality of Life-5 Dimensions; NIHSS, National Institutes of Health Stroke Scale; OSA, obstructive sleep apnea; REI, Respiratory event index; OR, odds ratio; CI, confidence interval.

0.007,95% CI 1.247–4.099 for mRS), (OR 1.228, p < 0.001,95% CI 1.057–1.336 for NIHSS), (OR 1.088, $p = 0.002$, 95% CI 1.032–1.146 for age), increase need of care EQ-5D (OR 1.820, $p = 0.037$,95% CI 1.036–3.198 for mRS), (OR 1.207, $p = 0.001$, 95% CI 1.081–1.349 for NIHSS), (OR 1.100, p < 0.001, 95% CI 1.043–1.160 for age) and worse BI (OR 1.727, $p = 0.046$, 95% CI 1.009–2.958 for mRS), (OR 1.214, $p = 0.01$,95% CI 1.087–1.355), (OR 1.076, $p = 0.003$, 95% CI 1.025–1.130 for age). The impaired admission mRS was found to be an independent risk factor for anxiety or depression EQ-5D (OR 1.678, $p = 0.038$, 95% CI 1.030–2.733). Elevated age predicted the need of medical aids (OR 1.082, $p = 0.001$, 95% CI 1.032–1.135) and fatigue (OR 1.043, $p = 0.028$, 95% CI 1.005–1.084) independently. Independent risk factors for the institutional care were impaired admission mRS (OR 2.126, $p = 0.021$, 95% CI 1.123–4.025) and age (OR 1.246, p = 0.001, 95% CI 1.099–1.413). The coronary artery disease was found to be an independent risk factor for insomnia (OR 3.802, $p = 0.011$, 95% CI 1.353–10.682).

Of the study patients 21 (15.4%) had CPAP-treatment. Of those, 90.5% used CPAP≥4 h per night and average use was six hours per night. There were more CPAP-users with REI ≥ 30/h compared to those who had CPAP and REI < 30/h (10.3% vs 5.1%, $p = 0.008$). The use of CPAP did not associate with decreased EQ-5D. Eleven (52.4%) patients with CPAP treatment and 77 (67.0%) patients without CPAP-treatment had decreased EQ-5D but there was no group difference ($p = 0.199$). The same result was found in groups REI ≥ 30/h (8/57.1% vs. 32/80.0%, $p = 0.093$) and REI < 30 (3/42.9% vs. 45/60.0%, $p = 0.379$). The usage of CPAP associated with a decreased risk of impaired usual activities (OR 0.190, 95% CI 0.042–0.857, $p = 0.031$).

4. Discussion

Our prospective study showed that seven years post-stroke activities of daily life and functional ability were decreased in those ischemic stroke patients who had severe OSA compared to others. The overall QOL tended to be impaired in patients with severe OSA and their mobility domain of EQ-5D was worse than in the other group. Furthermore, we pointed out that patients having severe OSA had more problems with walking and needed medical aids more often than others. Though severe OSA was not an independent risk factor for functional ability, whereas higher BMI was an independent risk factor for impaired EQ-5D and worse pain EQ-5D. Of note, CPAP treatment associated with an impaired risk of decreased usual activities. There was no difference between the groups in fatigue, mean FSS-9, mean ESS, prevalence of insomnia and mean insomnia severity index. The depression rate was low and equal between the groups.

At admission our ischemic stroke patients with severe OSA were older, had higher BMI, experienced more coronary artery disease and had more severe strokes compared to the other group patients. Further, after seven years follow-up four out of ten of our patients had severe OSA and they were more obese, had more hypertension and coronary artery disease than those in the other group. Those findings are in line with the previous study by Bassetti et al. [3]

In our study, the increased BMI predicted independently the risk for impaired EQ-5D and worse pain EQ-5D. Our findings are in line with previous studies. A meta-analysis in which adults with higher than normal BMI had significantly reduced physical quality of life with a clear dose-response relationship [32]. Obesity and a BMI are found to associate with impaired functional capacity and reduced quality of life in patients with chronic pain conditions [33].

In our study, the CPAP-treatment had positive effect only on usual activities domain in QOL. One recent study reported an improvement in QOL but not in mRS in ischemic stroke patients with good CPAP adherence [15], although also an improvement in functional recovery after stroke with CPAP-treatment has been reported [14]. Because untreated OSA patients tend to have poor recovery and high mortality risk after an ischemic stroke [4,5] we consider it is important to have a CPAP trial in order to find out those patients who may benefit from CPAP treatment. Moreover, recently a large study of older adult Medicare beneficiaries reported $396 reduced per-member per-month costs over 24 months in CPAP adherent OSA patients with stroke compared with non-adherent ones [34].

Our finding, that the everyday ability to act and functional outcome were worse in ischemic stroke patients with severe OSA is in line with most previous studies [3,35–38]. According to the former studies the ability to act or BI score was observed to be less satisfactory during 12 months post-stroke in patients with sleep apnea [7,35,36]. In our study mean BI was lower in patients with severe OSA than in those with less severe. We observed a group difference: half of our patients with severe OSA and two out of ten without severe OSA reported dependency in activities of daily living. In the whole study group 68.4% of the stroke survivors were independent in daily activities with a maximum score of 100 in the Barthel Index, and our results are comparable to one earlier study from Sweden [39]. We found out that severe OSA was associated to decreased BI, and the severity of stroke increased the risk of decreased BI. The good outcome has been defined as mRS scores 0–2 [40]. Of our patients, in 69.9% pre-and post-stroke functional ability was in good level but worse in severe OSA patients compared to those without severe OSA is in line with most earlier studies [3,15,38] with exception of two studies [4,13]. Some hypotheses have been put forward to explain the link between sleep apnea and stroke recovery: cerebral hypoperfusion or blood pressure variability related to sleep apnea could enlarge the penumbra area immediately after a stroke [36], or changes in cerebral blood and brain plasticity [35]. Recent study pointed out that in general the consequences of stroke were more severe after five years compared with at one year and they observed correlation between stroke-related disability and QOL [41]. One fifth of all our patients were still working seven years post-stroke and our results are comparable to the earlier study by Carlsson et al. [42] although even higher working rates has been reported [43,44].

However, we showed that post-stroke QOL was still in good level after seven years, and stroke severity and severe OSA did not increase the risk to decreased QOL which is in line with previous studies [7,39]. Our results showed that in EQ-5D questionnaire self-care, usual activities, pain or discomfort and anxiety or depression domains were in good level without group differences. We pointed out that only the mobility domain of EQ-5D was worse in patients with severe OSA compared to those with less severe OSA, which is in line with previous study [41]. Our finding that 62.5% of the study patients were without walking problems is comparable to the result from the previous study [39]. The walking was normal in half of severe OSA patients and in the other group even 70% had no problems with walking. One fourth of our stroke patients had problems with self-care and seven out of ten of our patients were without problems in usual activities domain and these results are comparable to the former results [39]. Pain and discomfort was experienced by 39% in this study and eight out of ten of our patients were without anxiety contrary to the previous studies with lower rates [39,45].

In agreement with previous studies, only tenth of our patients needed institutional care post-stroke and the need of institutional care was not affected by stroke severity or sleep apnea severity [39]. One third of all our patients needed medical aids, which was a higher proportion than reported in the earlier study from India [46]. We pointed out that severe OSA was associated to the increased need of the mobility aid while nearly half of our stroke patients with severe OSA required medical aids and only fifth of those without severe OSA.

In agreement with our study, a previous study also reported that one third suffered from post-stroke fatigue [47] but two studies reported lower or higher rates [42,48]. In this study stroke severity and severity of sleep apnea did not influence on post-stroke fatigue. According to recent study post-stroke fatigue is associated with decreased QOL and symptoms of depression [20].

We observed that one out of five had post-stroke depression and this

is in line with the study from England [49], while some studies reported higher rates [39,50]. None of our patients were extremely anxious or depressed. After seven years we showed notably increase in depression rates from baseline in both study groups, possibly due to decreased physical performance or the stroke itself. None of those with severe OSA were depressed at admission and after seven years 16.5% had post-stroke depression and the patients without severe OSA had sevenfold increase in depression rates within seven years. The post-stroke-depression was not affected by stroke severity or sleep apnea severity.

One third of our ischemic stroke patients had insomnia, which is in line with the earlier study [16] whereas one study reported lower rate than ours [17]. The sleep apnea severity and stroke severity did not increase the risk of post-stroke insomnia. The increase in diagnosis of insomnia after 7 years follow-up among our patients was threefold in the whole group and the increase was higher in severe OSA group. The increase in insomnia rates within follow-up might be due to older age, functional difficulties, or comorbidities. The former observation from Hongkong pointed out that four out of ten of stroke survivors experienced insomnia and had a reduced overall QOL [51]. Our finding that pre-and post-stroke ESS scores were low, and did not correlate with the presence of sleep apnea, is in line with former study [13] and contrary to another study which showed that stroke patients with REI $\geq$ 30/h had higher ESS scores than those with REI $<$ 10/h [3].

Our result, that one third of our patients did not survive is comparable to most previous studies [39,45], with exception of one former study with lower mortality rate than ours [52]. One patient did not want to participate in the seven years follow-up study resulting in 136 of the original 204 study patients. Our sample size is larger than in most recent studies [20,39,52], with one exception [45].

Our study has several strengths. Our observational, prospective, real-life single center study had one of the largest sample size of studies addressing years of post-stroke outcome. Of alive study patients 99.3% participated after seven years follow and none was lost to follow-up. Other studies have reported lower response rate and higher drop off rates than ours [39,45,53]. All our study patients were interviewed by the same investigator. Only a few studies have evaluated sleep apnea among ischemic stroke patients and their ability to act, QOL and fatigue over five years [39,54].

There are some limitations in our study. We could not evaluate the change in pre-and post-stroke QOL, functional ability, and fatigue, because we did not do the evaluation of our patients` EQ-5D, BI and FSS-9 in the acute phase of ischemic stroke. Only 15.4% of our patients used CPAP and we could see only benefit in usual activities domain, but higher numbers of CPAP-users would give more data of advantages of this sleep apnea treatment. This data did not provide information on whether a patient's retirement was due to age, stroke, or disability. This was a single-center study. It may be possible, that our results represent only situation in Finland.

5. Conclusions

The main finding of our study was that severe OSA was associated with the decreased functional ability as assessed by BI and the decreased mobility and the increased need of mobility aid in ischemic stroke patients. There is a health care provider system with a network of cerebrovascular support persons in the District of the Northern Ostrobothnia, which could partly explain the better QOL in our study than in some other studies. Furthermore, we showed, that the severe the stroke according to baseline NIHSS scores, the more impaired were BI, self-care, usual activities, and increased need of care. Only 15.4% of our patients used CPAP and we could see only benefit in usual activities domain, but higher numbers of CPAP-users would give more data of advantages of this sleep apnea treatment. However, since cardiorespiratory polygraphy and CPAP treatment compose only a minor part of the total health care costs of stroke patients, we consider screening and treatment of OSA feasible not only on humanitarian grounds but also in terms of health care costs [34].

Our study pointed out that, severe OSA decreased QOL after seven years. Screening of sleep apnea is important because the CPAP seemed to improve QOL in usual activities domain in those with severe OSA.

CRediT authorship contribution statement

Jaana K. Huhtakangas: Writing – review & editing, Writing – original draft, Visualization, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Juha Huhtakangas:** Writing – review & editing, Writing – original draft, Visualization, Supervision, Resources, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. **Marianne Haapea:** Writing – review & editing, Formal analysis, Data curation. **Tarja Saaresranta:** Writing – review & editing, Supervision, Resources, Methodology, Investigation, Formal analysis, Data curation, Conceptualization.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Data availability

The data that support the findings of this study are not publicly available due to patient data.

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