ACTA MEDICA SALINIANA

LOCALIZATION AND TYPE OF ACUTE STROKE IN RELATION TO SLEEP APNEA

Biljana Kojić, Zikrija Dostović, Omer Ć. Ibrahimagić, Dževdet Smajlović, Renata Hodžić, Amra Iljazović

ISSN 0350-364X

DOI: 10.5457/631

Biljana Kojić, Zikrija Dostović, Omer Ć. Ibrahimagić, Dževdet Smajlović, Renata Hodžić, Amra Iljazović

Affiliations:
Department of Neurology, University Clinical Center Tuzla, Bosnia and Herzegovina

Received:
15.12.2021.

Accepted:
15.11.2022.

Corresponding author:
Biljana Kojić
Address: Dr Ibre Pašića bb.75000 Tuzla, Bosnia and Herzegovina
Tel: +387 61 64 23 19
E-mail:biljana.kojic1@gmail.com

Funding: none

Competing interests: none

ABSTRACT

Background: More than 50% of stroke patients have sleep-disordered breathing.

Aim: To determine whether the location, side of stroke and type of stroke affect the occurrence of sleep apnea.

Patients and methods: Of the 500 patients with the first stroke treated at the Neurology Clinic for one year, 110 (22%) had sleep apnea. Acute stroke has been verified either by computerized tomography or magnetic resonance imaging of the brain. The mean age of subjects with apnea was 65.13 ± 9.27 years. The control group consisted of the same number of patients without apnea (n=110) and without a statistically significant difference in patient age and sex distribution.

Results: The largest number of patients with and without apnea had ischemic stroke 83.6%, while 16.4% of patients had hemorrhagic stroke. There was no statistically significant difference in type of stroke between the groups. With apnea, the largest number had a lesion in two or more places 51.8%, as well as without apnea 45.45%, but the difference was not statistically significant. The largest number of patients with apnea, had lesions in right hemisphere (44/40%), and then followed both (40/36.4 %) and the left (26/23.6%) hemispheres. The largest number of patients without apnea had lesions in both (50/45.4%), left (32/29.1%) and right (28/25.5%) hemispheres. There is a statistically significant association between the localization of stroke in the right hemisphere and the apnea ($X^2 = 4.65$, $p = 0.03$).

Conclusion: There is a statistically significant association between the localization of stroke in the right hemisphere and the apnea.

Key words: Stroke, Sleep Apnea

INTRODUCTION

Sleep disordered breathing (SDB) is a disease of increasing importance and it is frequent in stroke patients. SDB is being recognized as an independent risk factor for several clinical consequences, including cardiovascular and cerebrovascular diseases. It is generally accepted that there exist an increased risk of stroke in persons that are diagnosed with sleep disordered breath. In the other hand SDB is revealed in the most of patients with stroke [1, 2]. Stroke can themselves generate SDB [3]. The presence of SDB is related to worst neurologic outcome after stroke. In the literature is reported that in hypertonic and diabetic patients with SDB timely recognition and treatment of SDB would prevent onset of stroke or reduce the severity of neurological deficit in case of stroke [1, 2]. Sleep apnea is the most frequent SDB found in 5%-15% of the population [4]. There are considered to be three types of sleep apnea disorders: obstructive, central, and mixed sleep apnea [5]. Obstructive sleep apnea (OSA), which affects about 10% to 20% of middle to older aged adults are characterized by the repeated obstruction of the upper airway during sleep that leads to complete cessation (apnea) or reduction (hyperpnea) of airflow, occurring irrespective of continued ventilatory effort. Before termination, these events lead to a decrease in blood oxygen saturation and an associated increase in carbon dioxide levels during longer events [6]. The termination of the apnea is often preceded by an arousal, which leads to sleep fragmentation and activation of the sympathetic nervous system. The former is hypothesized to be involved in the neurocognitive sequelae, whereas the latter leads to cardiovascular dysregulation. This process is identified as the possible cause for the daytime sleepiness and cardiovascular health and functioning problems witnessed in these individuals [7 - 9]. Stroke patients with OSA have a worse prognosis overall, but treatment with CPAP can have a significantly better impact on overall cognitive and other physical disabilities suffered after stroke [10]. The prevalence of stroke is decreasing in the USA compared to past two decades because of efficient health care, as well as the increased availability of advanced laboratory investigations, skilled neurologists, and stroke rehabilitation centers [11]. Severe OSA, which occurs when the Apnea Hypopnea Index (AHI) ≥15, shows higher prevalence of silent cerebrovascular lesions on MRI compared to less severe and moderate OSA. Therefore, polysomnography studies should be performed in all stroke patients regardless of the risk factors of OSA. Stroke mortality has decreased over the years in some of the countries which had the highest crude rate of mortality by stroke [12]. OSA is more common in stroke patients regardless of neurological damage in the brain areas and lesions, and the severity of OSA plays an important role in stroke incidence [13]. In OSA patients not only apneic/hypoxemic episodes cause oxidative stress and inflammatory damage to the blood vessels, but sympathetic system stimulation also releases catecholamines, and increased blood pressure leads to platelet aggregation and further damage to the vascular endothelium and progress to CVD and stroke [14].

Aim: To determine whether the location, side of stroke and type of stroke affect the occurrence of sleep apnea.

PATIENTS AND METHODS

This prospective study was conducted at the Clinic of Neurology of the University Clinical Center in Tuzla. The examined group of 110 patients in the acute phase of stroke sleep apnea was evaluated. The average age was 65.13 ± 9.27 years. Among them, it was 65 (59%) men. The number of patients with no apnea in the control group was the same as well as the gender ratio, with an average age of 64±8.69 years. The study group included patients who meet the following criteria: confirmation of a diagnosis of ischemic stroke or a hemorrhagic stroke by computed tomography (CT) and/or magnetic resonance imaging (MR) of the brain, pulmonological and neuropsychiatric assessment of sleep apnea performed within seven days after stroke, Mini Mental test (MMT) > 23, Glasgow coma scale (GCS) > 8, written consent for participation in the research by the patients or a close family member. Patients with a Glasgow score <8 on the day of neuropsychiatric examination were excluded from the study, as well as patients with epileptic seizures at the onset of stroke, with aphasia, with MMT< 23, with verified previous dementia/cognitive impairment (based on hetero anamnesis data from patients relatives, data from previous medical findings). Neurological, neuropsychiatric and pneumological tests were performed in all patients at five different periods: the first test - in the acute phase of stroke (first week of stroke), second test - one month after the stroke, third test- three months after stroke, fourth test - six months after stroke and fifth test - twelve months after stroke. In these periods, all patients were evaluated: The National Institute of Health Stroke Scale [15], Mini Mental Test [16], The Sleep and Snoring Questionnaire Test [17]. The Berlin Questionnaire Test [18], The Epworth Sleepiness Scale [19], The Stanford Sleepiness Scale [20] and the General Sleep Questionnaire [21]. The findings of CT of the brain and MR of the brain were interpreted by a radiologist who was not familiar with the goals and hypotheses of the research and based on whose results were established: type of stroke, localization of the lesion, and lesion size. The research included the registration of the following socio-demographic characteristics: gender and age.

Methods / Instruments

Glasgow coma scale

Observation and examination included three areas that were ranked according to the given instructions and thus three scores were obtained, one for each area; eye opening, best verbal response and motor response. These three scores were added into results which represents the Glasgow Coma Scale that ranges from 3 (most severe degree of coma) to 15 (normal consciousness). In relation to the brain lesion, the score is classified into three stages: severe lesion - if the score is 3 to 8, moderate lesion - if the score is 9-12 and mild lesion - if the score is 13 to 15.

Stroke Scale of the National Institutes of Health

Neurological deficit was measured by the NIHS scale, a graded neurological scale that examined the state of consciousness, visual field defects, bulbomotor and facial nerve function, motor and sensory impairment, ataxia, speech function, and neglect phenomenon. This scale is one of the most commonly used scales in research, but also in clinical work. The score ranged from 0 to 42, with the highest score indicating the most severe neurological deficit.

Mini-Mental State

In clinical practice, Mini-Mental State is the most widely used instrument for evaluating disorders of intellectual efficiency and the presence of intellectual deterioration. It has proven to be a valid, highly reliable test, sensitive to changes over time. It consists of examining different cognitive areas. The total score ranged from 0 (maximum cognitive deficit) to a maximum of 30 (no cognitive deficit). Different degrees of cognitive dysfunction (between these endpoints) correspond to the following scores: a score <10 - severe dementia, a score between 10 and 20 - moderate dementia, a score between 21 and 25 - mild dementia, score 26 which is a borderline score according to dementia and score >27 - no dementia.

The Sleep and Snoring Questionnaire Test

The Snoring and Sleep Apnea Questionnaire consists of 12 questions answered with yes or no. The scale was filled in by the examiner. Affirmative answers to questions 1, 3, 4, 8 and 9 are a high indicator for sleep apnea.

Berlin Questionnaire Test

The Berlin questionnaire included 10 questions on risk factors for sleep apnea, including body weight, snoring, breathing pauses, drowsiness on walking or during the day and hypertension. The scale was filled by the examiner by circling the offered answers. The ranking of the answers is gradual: 0 = never or almost never, 1 = 1 to 2 times a month, 2 = 1 to 2 times a week, 3 = 3 times a week and 4 = almost every day.

Epworth Sleepiness Scale

The Epworth scale is designed to identify sleep problems. It consists of 4 parts that analyze drowsiness, sleep apnea/snoring, narcolepsy and other disorders. Scoring and analysis were performed according to the attached key. The ranking of the answers is gradual: 1 = rarely or never, 2 = sometimes, 3 = often, 4 = mostly. The scale was filled in by the examiner.

Stanford Sleepiness Scale

The Stanford Sleepiness Scale is designed to self fatigue and measure drowsiness. It consists of 7 levels that describe the degree of drowsiness. It is used along with other scales when diagnosing sleep disorders and narcolepsy. If the patients score is above 3, he has serious sleep problems. The scale was filled by the examiner.

General sleep questionnaire

The General Sleep Questionnaire is adapted from the General Sleep Questionnaire and Vigilance Assessment from Stanford University which is also used at the Center for Sleep Disorders, New Jersey. This questionnaire contains the following data: socio demographic (name, age, gender, and occupation), sleep pattern data, daytime sleepiness, chronic somatic diseases, and health data. The questionnaire has a total of 46 questions. The scale is filled in by the examiner with yes or no. The general questionnaire analyzed the following risk factors. Hypertension (systolic blood pressure >140 mm Hg, or diastolic >90 mm Hg or both), diagnosed at least two years before the stroke, or documented treatment of hypertension, heart disease (angina pectoris, myocardial infarction, arterial fibrillation, and consecutive heart failure) diagnosed by an internal medicine specialist or a cardiologist. Diabetes mellitus is defined by the use of drugs for diabetes before stroke or a documented blood glucose concentration >7 mol /L, hyperlipidemia (if cholesterol >5, ALDL>3 and triglycerides >2, smoking at least 10 cigarettes per day for months, and body mass index (BMI), which represents the ratio of body weight of the patient (kg/m2) and whose value was included in four categories. BMI categories were: malnutrition <18.5, normal weight = 18.5 - 24.9, elevated = 25-29.9 and obesity ≥30.

Statistical Analysi

Numerical test results were statistically processed, analyzed and compared, to obtain answers to questions formulated within the research objectives. From the basic descriptive statistical parameters, standard statistical methods were used for qualitative and quantitative evaluation of the obtained results: absolute numbers, relative numbers, arithmetic mean (X), standard deviation (SD), and range of values. When testing the statistical significance of main differences, the standard Student T-test was used. Descriptive statistics were processed using the X^2 (Hi - square test) and the proportional test. When testing statistical hypotheses, a significance level of p <0.05 was taken. All calculations were performed using the Arcus Quickstadt Biomedical statistical data processing program as well as the long rank test with p < 0.05 considered significant. The research was approved by an Ethics Committee of the University Clinical Center Tuzla.

RESULTS

Among 500 patients with the first ever stroke, there were 110 (22%) patients with sleep apnea whose mean age was 65.13 ± 9.27 years, and (65 or 59%) were men. The control group consisted of the same number of patients without apnea (n = 110), mean age 64.94 ± 8.69 years, with the same sex distribution (m = 65; f = 45). There is no statistically significant difference in the age of patients with or without apnea, neither in men (t = -0.46, p = 0.65) or in women (t = 0.32, p = 0.75), nor in total men and women (t = -0.16, p = 0.88). There is no statistically significant difference in the age of patients with (t=0.75, p=0.46) or without apnea (t=0.27, p=0.79) (Table 1).

Table 1. Distribution of patients with and without apnea in relation to age and gender

Age (years)	With apnea Men N %		Women N %		Without apnea Men N %		Women N %		Total With N %		Without N %
41-50	1	1.5	3	6.6	2	3.1	3	6.6	4	3.6	5
51-60	16	24.6	12	26.7	15	23.1	12	26.7	28	25.5	27
61-70	26	40.0	18	40.0	27	41.5	18	40.0	44	40.0	45
>70	22	33.9	12	26.7	21	32.3	12	26.7	34	30.9	33
Total	65	100.0	45	100.0	65	100.0	45	100.0	110	100.0	110

with apnea (t=0.75, p=0.46) without apnea (t=0.27, p=0.79)

The largest number of patients with and without apnea had an ischemic stroke (92/83.6%), while 18 (16.4%) of patients had a hemorrhagic stroke. Of these, there were 56 (86.2%) men and 36 (80%) women with ischemic and 9 (13.8%) men and 9 (20%) women with hemorrhagic stroke, but the difference was not statistically significant (p> 0.05) (Table 2).

Table 2. Distribution of patients with and without apnea by gender and type of stroke

Stroke	With apnea				Without apnea				Total			
	Men N %		Women N %		Men N %		Women N %		Men N %		Women N %	
Ischemic	56	86.2	36	80	56	86.2	36	80	92	83.6	92	
Hemorrhagic	9	13.8	9	20	9	13.8	9	20	18	16.4	18	
Total	65	100.0	45	100.0	65	100.0	45	100.0	110	100.0	110	

with – without apnea (p> 0.05)

Table 3 shows distribution of patients with and without apnea by gender and localization of stroke. The largest number of patients with apnea had a lesion in two or more places (57/51.8%), followed by patients with a lesion in the temporal lobe (17/15.5%). The largest number of patients without apnea had a lesion in two or more places (50/45.45%), followed by patients with a lesion in the temporal lobe (16/14.54%). In the group of the patients with apnea it was determined statistically more frequent lesions in two or more places that in the brainstem (X^2= 40.88, p <0.0001). The chance of apnea is 8.78 (95% CI: 4.17-19.43) times higher in the case when the localization of the lesion is in two or more places, than in patients with a lesion in the brainstem. In the group without apnea, the largest number of patients had a lesion in two or more places compared to brainstem lesions (X^2 = 28.83, p <0.0001). There was no statistically significant difference in the localization of stroke in the group of patient with and without apnea (p> 0.05) (Table 3).

Table 3. Distribution of patients with and without apnea by gender and localization of stroke

Stroke localization	With apnea				Without apnea				Total			
	Men		Women		Men		Women		With		Without	
	N	%	N	%	N	%	N	%	N	%	N	%
Frontal lobe	7	10.8	1	2.2	7	10.8	5	11.1	8	7.3	12	
Temporal	11	16.9	6	13.3	11	16.9	5	11.1	17	15.5	16	
Parietal	5	7.7	3	6.7	6	9.2	5	11.1	8	7.3	11	
Occipital	1	1.5	0.0	0.0	1	1.5	1	2.2	1	0.9	2	
Cerebellum	4	6.2	3	6.7	4	6.2	2	4.4	7	6.3	6	
Brain stem	8	12.3	4	8.9	7	10.8	6	13.3	12	10.9	13	
Two or more places	29	44.6	28	62.2	29	44.6	21	46.7	57	51.8	50	
Total	65	100.0	45	100.0	65	100.0	45	100.0	110	100.0	110	

with - without apnea (p>0.05)

According to the side of acute stroke, the largest number of patients with apnea had lesions in right (44/40%), both (40/36.4%) and the left (26/23.6%) hemispheres. The largest number of patients without apnea had lesions in both (50/45.4%), left (32/29.1%) and right (28/25.5%) hemispheres. There is statistically significant association between the localization of stroke in the right hemisphere and the occurrence of apnea (X^2 = 4.65, p = 0.03). The chance of stroke on the right side is 1.95 times (95% CI: 1.06-3.62) higher in patients with than in patients without apnea (Table 4).

Table 4. Distribution of patients with and without sleep apnea according to the gender and side of stroke

Side of lesion	With apnea				Without apnea				Total			
	Men		Women		Men		Women		With		Without	
	N	%	N	%	N	%	N	%	N	%	N	%
Left side	17	26.2	9	2.0	19	29.2	13	28.9	26	23.6	32	
Right side	30	46.1	14	31.1	17	26.2	11	24.4	44	40.0*	28	
Both sides	18	27.7	22	48.9	29	44.6	21	46.7	40	36.4	50	
Total	65	100.0	45	100.0	65	100.0	45	100.0	110	100.0	110	

left side (X^2=0.59, p=0.44), both sides (X^2=0.0, p=1) *X^2=4.65, p=0.03 (right side)

DISCUSSION

The results of many studies underline the association between sleep-disordered breathing (SDB) and cerebrovascular disorders. SDB, mostly obstructive sleep apnea syndrome (OSAS), is believed to be an independent risk factor of stroke and is related to poor outcome and increased long-term stroke mortality. Wierzbicka et al. reported that SDB was present in 27 (62.8%) patients with stroke and transient ischemic attack, stratified into those with AHI 5-10 (10 patients), 10-20 (8 patients), and AHI>20 (9 patients). In 15 patients, there was an increase in AHI >or=5 on assuming the supine position [22]. Apneas during sleep (sleep apnea - SA) are present in about 1% of the total population. Aging increases a prevalence of SA and it is three times more often in a population that is older than 40 years of age. In the adults, obstructive sleep apnea (OSA) is more often present compared to the central sleep apnea (CSA) (84% vs. 0.4%). Mixed sleep apnea (MSA) is a combination of two forms and occurs in 15% of all population. SA is found in 50-70% of patients with stroke [23]. The severity of the patient's OSA apnea-hypopnea index (AHI≥30) plays an important role in the development of ischemic stroke, especially in older patients [24]. The prevalence of stroke is strongly associated with OSA; particularly, the severity of OSA plays a significant role in the development of stroke [25]. Stroke incidence increases with the severity of OSA [26]. OSA is highly prevalent in stroke patients who are not treated with adequate continuous positive air pressure (CPAP) treatment [27]. In our study 22% patients with acute stroke had SA. The mean age of patients with apnea was 65.13 ± 9.27 years, whereas in the control group the mean age of patients was 64.94 ± 8.69 years. According to Janssens et al. the prevalence of apnea increases with age and ranges from 11% to 62%, something that is supported in our study. Minoguchi et al. reported that SA is an independent predictor of increased risk of stroke and mortality in elderly patients [28]. In a study of 741 patients with AHI> 10, the presence of apnea was verified in 3.3% in the 20-90 years, with a maximum prevalence in the 45-64 years [29]. Therefore, it has been suggested that the prevalence of apnea increases with age, but that the clinical significance and severity of apnea decreases [30]. A higher incidence of apnea in older age groups has also been found in several other studies stating that aging alters pharyngeal anatomy and functioning of pharyngeal dilator muscles and increases the risk of apnea and stroke in elderly populations, something that is consistent with the findings in our study [31, 32]. The majority of patients in our study were man (59%), which corresponds to the results of other studies because men are more susceptible to the occurrence of apnea due to the reduced threshold of carbon dioxide sensitivity compared to women [33]. Redline et al. documented the ratio of men and women in the community with a range (2 to 3: 1. to 8: 1) [34]. OSA is more common in stroke patients regardless of neurological damage in the brain areas and lesions, and the severity of OSA plays an important role in stroke incidence [13]. One prospective longitudinal study examining the elderly (age 70–100) shows that patients with severe OSA (AHI≥30) demonstrated higher incidence of stroke compared to patients without OSA [24]. Stroke patients with OSA have a worse prognosis, experiencing a more prolonged hospitalization and spending more time in rehabilitation [35]. Redline et al. reported that men with AHI >19 have a hazard ratio of 2.8 for stroke, and that for every single-measure- unit risk factor for stroke and death in men increases for 6% [36]. In our study, ischemic stroke was verified in 92 (83.63%) and hemorrhagic stroke in 18 (16.36%) patients with apnea. Similar results were found in other studies. OSA has been documented to be present in 73–93% patients [37, 38] of ischemic stroke patients, compared with a community prevalence of 21% [39]. Patients with acute ischemic stroke and OSA have worse outcomes than those without OSA, including increased risk of early neurological worsening, mortality, decreased functional recovery, nonfatal cardiovascular events, longer hospital stays, delirium, and depressed mood [40-45]. In a prospective study conducted on 152 patients with acute stroke, it was confirmed that patients with acute IS have a high incidence of sleep-disordered breathing 72%, and that in many cases respiratory disorders preceded ischemic stroke including TIA [46]. In Pasic study they also found a relationship between SA and stroke among 200 stroke patients, where 40.5% of patients had OSA, and the majority, 76.8%, had ischemic stroke [47]. Sleep apnea is a separate risk factor that correlates with poor outcome and increased long-term mortality in stroke patients. Hu et al. reported that 63% of patients with ischemic stroke had also SA and 12.5% were without SA [48]. According to Herman et al. SA is observed in 50–59% of stroke patients. Similarly, SA is documented in 62% of patients (Iranzo et al.), as well as in 77.6% of patients (Rolla et al.). All these studies documented higher number of patients with SA compared to our study because they excluded patients with severe speech disorders. In addition, they used polysomnography for the diagnosis of SA, whereas we have used questionnaires in our study [49, 40, 50]. The largest number of patients in our study with apnea had a lesion in two or more places 57 (51.8%), followed by patients with a lesion in the temporal lobe (17/15.5%). However, no statistically significant difference in the frequency of stroke lesions was found in patients with and without apnea (p> 0.05). Other studies documented similar results to our study with regard to the localization of stroke and apnea. In a study of 39 patients (15 women and 24 men, mean age 57 years) with the first acute stroke, of which 26 (67%) had SA a connection between respiratory problems in sleeping and localization of stroke could not be find [51]. In our study, no connection was found between the localization of stroke and SA (p = 0.58) [47]. In their study on 161 stroke patients and SA, Parra et al. have also found no correlation between SA and the topographic location of neurological lesion [13]. In a study conducted in 27 patients with stroke (mean age: 66 +/- 10 years and BMI 24.4 +/- 4.4) they found apnea in 15 (59%). OSA was found in 53.3%, mixed in 40% and central apnea in 6.7% of patients. There was no statistically significant difference that would indicate an association between apnea and the localization of stroke [52]. In relation to the side of stroke in our study, the largest number of patients with apnea had lesions in the right hemisphere (44/40%), both (40/36.4%) and left (26/23.6%) side. The largest number of patients without apnea had lesions in the both side (50/45.4%), left (32/29.1%) and right (28/25.4%). However, there is a statistically significant difference in the frequency of stroke on the right side of the brain in patients with apnea compared to patients without apnea (X^2 = 4.65, p = 0.03). The chance of stroke on the right side is 1.95 times (95% CI: 1.06-3.62) higher in patients with apnea than in patients without apnea in our study. Similar study was conducted in the Łabuz - Roszak et al. which reported that 23 (85.5%) surviving SA patients had a lesion (s) in the left hemisphere, but this difference was not significant (X^2= 4.37, p = 0.11). Patients without SA 48 (96%) had lesion (s) on both sides, but this difference was not significant (X^2 = 2.22, p = 0.33) [52]. Wierzbick et al. analyzed 43 patients with stroke and SA and not verified significant correlation between the apnea and side of stroke [53]. Pasic also did not found significant correlation between the apnea and side of stroke (left 33%, right 39.5%, both 27%) (X^2= 1.98, p=0.161) [47]. According to the fact that our Department is not specialized in sleep disorders we were not able to do polysomnografy and AHI index, which can be characterized as a lack of research. By searching a database in our country and region, we found that there are not many publications on sleep disorders after stroke, which motivated us more to do this research.

CONCLUSION

In this study, almost quarter of stroke patients had sleep apnea. In patients with sleep apnea, stroke was more frequent in the right hemisphere.

REFERENCES

1. Mohsenin V. Obstructive sleep apnea: a new preventive and therapeutic target for stroke: a new kid on the block. Am J Med 2015; 128:811–816.
2. Lyons OD, Ryan CM. Sleep Apnea and Stroke. Can J Cardiol. 2015; 31:918–927. 3.
3. Iyer SR, Iyer RR. Sleep, ageing and stroke--newer directions in management of stroke. J Assoc Physicians India 2010; 58:442–446.
4. Dincer HE, O'Neill W. Deleterious effects of sleep-disordered breathing on the heart and vascular system. Respiration 2006; 73:124–130.
5. Pinel JPJ. Biological psycology. Jastrebarsko: Naklada Slap 2002.
6. Vgontzas AN, Liao D, Pejovic S, et al. Insomnia with short sleep duration and mortality: the Penn State cohort. Sleep 2010; 33(9):1159–64.
7. Marin JM, Agusti A, Villar I, et al. Association between treated and untreated obstructive sleep apnea and risk of hypertension. JAMA 2012; 307(20):2169–76.
8. Nieto FJ, Young TB, Lind BK, et al. Association of sleep-disordered breathing, sleep apnea, and hypertension in a large community-based study. Sleep Heart Health Study. JAMA 2000; 283(14):1829–36.
9. Peppard PE, Young T, Palta M, et al. Prospective study of the association between sleep-disordered breathing and hypertension. N Engl J Med 2000; 342(19):1378–84.
10. Disler P, Hansford A, Skelton J, et al. Diagnosis and treatment of obstructive sleep apnea in a stroke rehabilitation unit: a feasibility study. Am J Phys Med Rehabil 2002; 81(8):622–625.
11. Jehan S, Farag M, Zizi F, Pandi-Perumal SR, Chung A, Truong A, Girardin- Jean-Louis G, Tello D.Obstructive sleep apnea and stroke.Sleep Med Disord. 2018; 2(5): 120–125.
12. Nishibayashi M, Miyamoto M, Miyamoto T. Correlation between severity of obstructive sleep apnea and prevalence of silent cerebrovascular lesions. J Clin Sleep Med 2008; 4(3):242–247.
13. Parra O, Arboix A, Bechich S, et al. Time course of sleep-related breathing disorders in first-ever stroke or transient ischemic attack. Am J Respir Crit Care Med 2000; 161(2 Pt 1):375–380.
14. Eisensehr I, Ehrenberg BL, Noachtar S, et al. Platelet activation, epinephrine, and blood pressure in obstructive sleep apnea syndrome. Neurology 1998; 51(1):188–195.
15. Lyden PD, Lu M, Levine S, Brott TG &Broderick J: A modified National Institutes of Health Stroke Scale for use in stroke clinical trials. Preliminary reliability and validity. Stroke 2001; 32:1310-1317.
16. Folstein MF, Folstein SE & Mc Hugh PR: Mini - Mental State: A practical method for grading the cognitive of patients for the clinical. J Psychiatry res 1975; 12:189-198.
17. Denbar AM. Sleep and Breathing. Springer Berlin/Heidelberg 2002: 125-128.
18. Netzer CM, Clark K, Strohl KP. Using the Berlin Questionnaire to identify patients at risk for the sleep apnea syndrome. Ann Intern Med 1999; 131: 485-491.
19. Johns MW. A new method for measuring daytime sleepiness, The Epworth Sleepiness Scale. Sleep 1991; 14: 540-545.
20. Hoddes E, Zarcone V, Smythe H, Phillips R, Dement W. Quantification of sleepiness: a new approach. Phychophysiology 1973; 10: 431-436.
21. Douglass AB, Bornstein R, Nino-Murcia G, Keenan S, Miles L, Zarcone VP, Guilleminault C, Dement WC. The Sleep Disorders Questionnaire. Sleep 1994; 17 (2): 160-167.
22. A Wierzbicka A , R Rola R, Wichniak A, Richter P, Ryglewicz D, Jernajczyk W. The incidence of sleep apnea in patients with stroke or transient ischemic attack. J PhysiolPharmacol 2006; 57 Suppl 4:385-90.
23. Young T, Peppard PE, Gottlieb DJ. Epidemiology of obstructive sleep apnea: a population health perspective. Am J Respir Crit Care Med 2002; 165(9):1217–1239.
24. Munoz R, Cantolla JD, Martínez VE, et al. Severe sleep apnea and risk of ischemic stroke in the elderly. Stroke 2006; 37:2317–2321.
25. Arzt M, Young T, Finn L, et al. Association of sleep-disordered breathing and the occurrence of stroke. Am J Respir Crit Care Med 2005; 172(11):1447–1451.
26. Harbison J, Ford GA, James OF. Sleep-disordered breathing following acute stroke. QJM 2002; 95(11):741–747.
27. Hui DS, Choy DK, Wong LK. Prevalence of sleep-disordered breathing and continuous positive airway pressure compliance: results in Chinese patients with first-ever ischemic stroke. Chest 2002; 122(3):852–860.

28. Janssens JP, Pautex S, Hilleret H, Michel JP. Sleep disordered breathing in the elderly. Sleep 2000; 12 (6): 417-429.
29. Minoguchi K, Yokoe T, Tazaki T, Minoguchi H, Oda N, Tanaka A. Silent brain infarction and platelet activation in obstructive sleep apnea. Am J Respir Crit Care Med 2007; 175: 612-627.
30. Bixler EO, Vgontzas AN, Ten Have T, Tyson K, Kales A. Effects of age on sleep apnea in men: Prevalence and severity. Am J Respir Crit Care Med 1998; 157 (1): 144-148.
31. Martin SE, Mathur R, Marshall I, Douglas NJ. The effect of age, sex, obesity and posture on upper airway size. Eur Respir J 1997; 10 (9): 2087-2090.
32. Thurnheer R, Wraith PK, Douglas NJ. Influence of age and gender on upper airway resistance in NREM and REM sleep. J Appl Physiol 2001: 90 (3): 981-988.
33. Zhuo SQ, Yang XP, Chen YC, Tian XT, Lian H, Ou Q. Effect of obstructive sleep apnea syndrome on blood lipid and blood glucose in elderly hypertensive patients. Nan Fang Yi Ke Da XueXue Bao 2009; 29 (2): 330-332.
34. Redline S, Kump K, Tishler PV, Browner I, Ferrette V. Gender differences in sleep disordered breathing in a community-based sample. Am J Respir Crit Care Med Mar 1994; 149 (1): 722-726.
35. Kaneko Y, Hajek VE, Zivanovic V, et al. Relationship of sleep apnea to functional capacity and length of hospitalization following stroke. Sleep 2003; 26(3):293–297.
36. Redline S, Yenokyan G, Gottlieb JD, Shahar E, O'Connor GT, Resnick EH, West DM, Mark H. Sanders, Wolf AP, Estella M. Geraghty ME, Ali T, Lebowitz M, Naresh M. Obstructive Sleep Apnea - Hypopnea and Incident Stroke. Am J Respir Crit Care Med 2010; 182: 269-277.
37. Brown DL, Lisabeth LD, Zupancic MJ, Concannon M, Martin C, Chervin RD. High prevalence of supine sleep in ischemic stroke patients. Stroke a journal of cerebral circulation 2008; 39:2511–2514.
38. Noradina AT, Hamidon BB, Roslan H, Raymond AA. Risk factors for developing sleep-disordered breathing in patients with recent ischaemic stroke. Singapore medical journal 2006; 47:392–399.
39. Peppard PE, Young T, Barnet JH, Palta M, Hagen EW, Hla KM. Increased prevalence of sleep-disordered breathing in adults. American journal of epidemiology 2013; 177:1006–1014.
40. Iranzo A, Santamaria J, Berenguer J, Sanchez M, Chamorro A. Prevalence and clinical importance of sleep apnea in the first night after cerebral infarction. Neurology 2002; 58:911–916.
41. Good DC, Henkle JQ, Gelber D, Welsh J, Verhulst S. Sleep-disordered breathing and poor functional outcome after stroke. Stroke a journal of cerebral circulation1996; 27:252–259.
42. Sahlin C, Sandberg O, Gustafson Y, et al. Obstructive sleep apnea is a risk factor for death in patients with stroke: a 10-year follow-up. Archives of internal medicine 2008; 168:297–301.
43. Bassetti C, Aldrich MS. Sleep apnea in acute cerebrovascular diseases: final report on 128 patients. Sleep1999; 22:217–223.
44. Martinez-Garcia MA, Campos-Rodriguez F, Soler-Cataluna JJ, Catalan-Serra P, Roman-Sanchez P, Montserrat JM. Increased incidence of nonfatal cardiovascular events in stroke patients with sleep apnoea: effect of CPAP treatment.The European respiratory journal 2012; 39:906–912.
45. Sandberg O, Franklin KA, Bucht G, Gustafson Y. Sleep apnea, delirium, depressed mood, cognition, and ADL ability after stroke. Journal of the American Geriatrics-Society 2001; 49:391–397.
46. Bassetti C, Milanova M, Gugger M. Sleep-Disordered Breathingand Acute Ischemic Stroke. Stroke 2006; 37: 967-972.
47. Pašić Z. Sleep disorders in patients with stroke. Master's thesis. Faculty of Medicine, University of Tuzla, 2009.
48. Hu F, Willet W, Manson J. Snoring and risk of cardiovascular disease in women. J Am Coll Cardiol 2000; 35: 308-313.
49. Hermann DM, Bassetti CL. Sleep-related breathing and sleepwake disturbances in ischemic stroke. Neurology 2009; (73): 1313-1322.
50. Rola R, Wierzbicka A, Wichniak A, Jernajczyk W, Richter P, Ryglewicz D. Sleep related breathing disorders in patients with ischemic stroke and transient ischemic attacks: respiratory and clinical correlations. J Physiol Pharmacol 2007; 58(5): 575-582.
51. Bassetti C, Aldrich MS, Quint D. Sleep-Disordered Breathing in Patients With Acute Supra-and Infratentorial Strokes A Prospective Study of 39 Patients. Stroke 1997; 28: 1765-1772.
52. Labuz-Roszak B, Tazbirek M, Pierzchala K, Pierzchala W. Frequency of sleep apnea syndrome in patients with acute stroke. Pol MerkuriusznLek 2004; 16(96): 536-538.
53. Wierzbicka A, Rola R, Wichniak A, Richter P, RyglewiczD, Jernajczyk W. The incidence of sleep apnea in patients with stroke or transient ischemic attack. J Physiol Pharmacol 2001; 57(4): 385-390.