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# One Year Outcome of Patients with Acute Stroke and Sleep Apnea According to the Type and Localisation of Lesion

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## ABSTRACT

**The aim** of this study was to analyze one year survival outcome of the patients with sleep apnea in acute stroke in order to type and localisation of lesion. **Patients and Methods:** It was analyzed 110 patients with acute stroke (AS) and verified sleep apnea, treated at Department of Neurology, University Clinical Center Tuzla in the period December 2009 thorough may 2010. Acute stroke has been verified either by computerized tomography or magnetic resonance imaging of the brain. Average age was  $65.13 \pm 9.27$  years and it was 65 (59%) men. Number of participants with no apnea in control group was the same as well as sex distribution, with average age  $64 \pm 8.69$  years. **Results:** One year after acute stroke survived 78 (84.8%) patients out of 92 with apnea and ischemic stroke (IS). Otherwise, 13 (72.2%) patients survived out of 18 with hemorrhagic stroke (HS). Without apnea 88 (95.7%) patients who survived had IS and 16 (88.9%) HS. Survival of patients with IS and without apnea is significantly better than in patients with IS and apnea ( $X^2=5.46$ ,  $p=0.02$ ). Survival of patients with HS with/without apnea is not significantly different. Majority (51/87.9%) of 58 patients with apnea who survived had lesions at two or more locations. Otherwise, 12 (100%) patients out of 12 without apnea who survived had lesion in frontal lobe. Survival of patients with/without apnea is not statistically different in order to location of lesion. Concerning the side of stroke 23 (85.5%) patients with apnea who survived had lesion(s) in left hemisphere but this difference is not significant. Patients without apnea 48 (96%) had lesion(s) at both sides. **Conclusion:** Survival of patients without apnea in ischemic stroke is significantly better than in patients with apnea. Survival in patients with/without apnea in hemorrhagic stroke has no statistical difference. Localization and side of lesion do not have influence on survival. **Key words:** Stroke, Apnea, Localization, One year outcome.

## 1. INTRODUCTION

Sleep disorders breathing (SDB), presenting with obstructive (OSA), central (CSA), or mixed apneas (MSA), is present in 50%–70% of stroke patients (1). Furthermore, OSA is major sleep problem characterized by repetitive upper airway closure during sleep resulting in repeated reversible blood oxygen desaturation and fragmented sleep. OSA has been associated with a range of pathophysiological changes that impair cardiovascular function (2) including increased blood inflammatory markers and repeated rises in blood pressure during sleep. There is increasing evidence that OSA promotes the development of hypertension, stroke, myocardial infarction and premature death (3). SDB are isolated risk factor that is correlated with poor outcome and increased long-term mortality in patients with stroke (4). The prevalence of sleep apnea (SA) increases with age and is three times more common in adults over 40 years of age (5). In women, incidence increases after menopause. In women who use hormonal therapy fre-

quency of apnea is similar to period before menopause. SA prevalence among men 30 to 60 years of age is 10–20% (6).

## 2. THE AIM

The aim of this study was to analyze one year survival outcome of the patients with sleep apnea in acute stroke in order to type and localisation of lesion.

## 3. PATIENTS AND METHODS

It was analyzed 110 patients with acute stroke (AS) and verified sleep apnea, treated at Department of Neurology, University Clinical Center Tuzla in the period December 2009 thorough may 2010. Acute stroke has been verified either by computerized tomography or magnetic resonance imaging of the brain. Average age was  $65.13 \pm 9.27$  years and it was 65 (59%) men. Number of participants with no apnea in control group was the same as well as sex distribution, with average age  $64 \pm 8.69$  years. Patient selection was made consecutively, and clinical instruments for

assessment were: "The Sleep Disorders Questionnaire"(7), "Berlin Questionnaire to identify patients at risk for the sleep apnea syndrome"(8) and "The Epworth Sleepiness Scale" (9). Tests have been performed to all patients twice: first time at the admission to Department of Neurology and second time, one year after the stroke, previously been called and checked by phone. Statistical data was analyzed by standard Student's t-test,  $\chi^2$  test, Arcus Quickstat Biomedical statistical program, as well as Long rank test with  $p < 0.05$  considered significant.

#### 4. RESULTS AND DISCUSSION

Among five hundred patients with first ever stroke 110 (22%) had sleep apnea. Ischemic stroke was identified in 92 (83.63%), and hemorrhage in 18 (16.36%) patients. One year after acute stroke survived 78 (84.8%) patients out of 92 with apnea and ischemic stroke (IS). Otherwise, 13 (72.2%) patients survived out of 18 with hemorrhagic stroke (HS). Without SA survived 104 (94.5%) patients, 88 (95.7%) with ischemic stroke and 16 (88.9%) with hemorrhagic stroke. Survival of patients with IS and without apnea is significantly better than in patients with IS and apnea ( $\chi^2=5.46$ ,  $p=0.02$ ). Survival of patients with HS with/without apnea is not significantly different ( $\chi^2=2.1$ ,  $p=0.15$ ). This study shows that SA increases the risk of ischemic stroke (Table 1, 2).

Pašić (10) in study among 200 patients with stroke, 40.5% of patients had OSA, and most of them, 76.8% had an IMU. Sleep apnea is separated risk factor which correlates with bad outcome and increase long-term mortality in patients with stroke. Hu et al. (11) found that 63% of patients with IS have sleep apnea and 12.5% of patients without SA. According to Herman et al. (12) SA is observed in 50-59% of patients with stroke, Iranzo et al. (13) in 62% and Rolla et al. (14) in 77.6% what is higher than in our study because they

Survival rate with apnea (months)	Ischemic stroke N=92 100.0%	Hemorrhagic stroke N= 18 100.0%	Total N =110 100.0%
1	91 98.9	18 100.0	109 99.1
2	89 96.7	17 94.4	106 96.4
3	88 95.7	16 88.9	104 94.5
4	87 94.6	16 88.9	103 93.6
5	87 94.6	16 88.9	103 93.6
6	86 93.5	14 77.8	100 90.9
7	85 92.4	14 77.8	99 90.0
8	84 91.3	13 72.2	97 88.2
9	84 91.3	13 72.2	97 88.2
10	84 91.3	13 72.2	97 88.2
11	81 88.0	13 72.2	91 87.2
12	78 84.9	13 72.2	91 82.7

**Table 1. One-year survival rate with sleep apnea in order to type stroke.** \* $\chi^2=5.46$ ,  $p=0.02$  (Ischemic stroke with/without apnea),  $\chi^2=2.1$ ,  $p=0.15$  (Hemorrhagic stroke with/without apnea)

Survival rate without apnea (months)	Ischemic stroke N=92 100.0 %	Hemorrhagic stroke N= 18 100.0%	Total N =110 100%
1	92 100.0	18 100.0	110 100.0
2	92 100.0	16 88.9	108 98.2
3	91 98.9	16 88.9	107 97.3
4	90 97.8	16 88.9	106 96.4
5	90 97.8	16 88.9	106 96.4
6	90 97.8	16 88.9	106 96.4
7	90 97.8	16 88.9	106 96.4
8	90 97.8	16 88.9	106 96.4
9	90 97.8	16 88.9	106 96.4
10	89 96.7	16 88.9	105 95.5
11	88 95.7	16 88.9	104 94.5
12	88 95.7	16 88.9	104 94.5

**Table 2. One-year survival rate without sleep apnea in order to type stroke**

included patients with severe speech disorders, and polysomnography was used rather than questionnaires for the diagnosis of SA as in our study. Marin et al. (15) showed that in men, severe OSA (defined as AHI >30) significantly increases the composite risk of fatal and nonfatal cardiovascular events, including stroke. Munoz et al. (16) found after a follow-up time of 6 years (mean follow up time= 4.5 years), verified 20 ischemic strokes with SA representing an annual incidence of 11.28 per 1000 person-years. As expected, mortality was high at the end of the follow-up period 75/19% subjects.

Dyken et al. (17) found SA in 10 of 13 men with stroke (77%) and in only 3 of 13 male subjects without stroke (23%) ( $p=.0169$ ). Seven of 11 women with stroke (64%) had OSA, while only 2 of 14 female subjects without stroke (14%) had OSA ( $p=.0168$ ). The 4-year mortality for patients with stroke was 20.8%. All patients with stroke who died had OSA. In conclusion he stated that the patients with stroke have an increased incidence of OSA compared with normal sex- and age-matched control subjects. Hypoxia and hemodynamic responses to OSA may have predisposed these patients to stroke. Jaggi et al. (18) in a study among 1022 patients verified 697 (68%) with OSA. The OSA syndrome was associated with stroke or death from any cause (hazard ratio, 2.24; 95 percent confidence interval, 1.30 to 3.86;  $p=0.004$ ). After adjustment for age, sex, race, smoking, alcohol-consumption, body-mass index, and the presence or absence of diabetes mellitus, hyperlipidemia, atrial fibrillation, and hypertension, the OSA retained a statistically significant association with stroke or death (hazard ratio, 1.97; 95 percent confidence interval, 1.12 to 3.48;  $p=0.01$ ). Patients with an Apnea-Hypopnea index of 4 (Mild OSA) or greater were more than two times as likely to have a stroke or death

Survival rate (months)	Frontal lobe (n=5) N %		Temporal lobe (n=16) N %		Parijetal lobe (n=11) N %		Okcipital lobe (n=2) N %		Cerebellum (n=7) N %		Brainstem (n=11) N %		Two and more lesions (n=58) N %	
1	5	100.0	16	100.0	11	100.0	2	100.0	7	100.0	11	100.0	57	98.3
2	4	80.0	15	93.8	11	100.0	1	50.0	7	100.0	11	100.0	56	96.6
3	4	80.0	15	93.8	11	100.0	1	50.0	7	100.0	11	100.0	55	94.8
4	4	80.0	15	93.8	10	90.9	1	50.0	7	100.0	11	100.0	55	94.8
5	4	80.0	15	87.5	10	90.9	1	50.0	7	100.0	11	100.0	55	94.8
6	4	80.0	14	87.5	10	90.9	1	50.0	7	100.0	11	100.0	53	91.4
7	4	80.0	14	87.5	10	90.9	0.0	0.0	7	100.0	11	100.0	53	91.4
8	4	80.0	13	81.3	10	90.9	0.0	0.0	7	100.0	11	100.0	52	89.7
9	4	80.0	13	81.3	10	90.9	0.0	0.0	7	100.0	11	100.0	52	89.7
10	4	80.0	13	81.3	10	90.9	0.0	0.0	7	100.0	11	100.0	52	89.7
11	4	80.0	12	75.0	9	81.8	0.0	0.0	7	100.0	11	100.0	51	87.9
12	4	80.0	12	75.0	9	81.8	0.0	0.0	6	85.7	9	91.8	51	87.9

**Table 3.** One-year survival rate after stroke with sleep apnea according to the localisation of lesion. X2=1.8, p=0.88

Survival rate (months)	Frontal lobe (n=12)		Temporal lobe (n=16)		Parijetal lobe (n=11)		Okcipital lobe (n=2)		Cerebellum (n=6)		Brainstem (n=13)		Two and more lesions (n=50)	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%
1	12	100.0	16	100.0	11	100.0	2	100.0	6	100.0	13	100.0	50	100.0
2	12	100.0	16	100.0	10	100.0	2	100.0	6	100.0	12	92.3.	50	100.0
3	12	100.0	16	100.0	10	90.9	2	100.0	6	100.0	12	92.3	49	98.0
4	12	100.0	16	100.0	10	90.9	2	100.0	5	83.3	12	92.3	49	98.0
5	12	100.0	16	100.0	10	90.9	2	100.0	5	83.3	12	92.3	49	98.0
6	12	100.0	16	100.0	10	90.9	2	100.0	5	83.3	12	92.3	49	98.0
7	12	100.0	16	100.0	10	90.9	2	100.0	5	83.3	12	92.3	49	98.0
8	12	100.0	16	100.0	10	90.9	2	100.0	5	83.3	12	92.3	49	98.0
9	12	100.0	16	100.0	10	90.9	2	100.0	5	83.3	12	92.3	49	98.0
10	12	100.0	16	100.0	10	90.9	2	100.0	5	83.3	12	92.3	48	96.0
11	12	100.0	16	100.0	10	90.9	2	100.0	5	83.3	12	92.3	48	96.0
12	12	100.0	16	100.0	10	90.9	2	100.0	5	83.3	12	92.3	48	96.0

**Table 4.** One-year survival rate after stroke without sleep apnea according to the localisation of lesion p>0.05

event that those with an Apnea-Hypopnea index of 3 or less. Increased severity of the syndrome (Higher Apnea-Hypopnea Index) is associated with an incremental increase in the risk of stroke or death events. In conclusion he stated that the OSA significantly increases the risk of stroke or death from any cause, and the increase is independent of other risk factors, including hypertension. Arzt et al. (19) in a study that included 1475 patients with stroke and apnea patients and 1189 control group after 4 years of follow-find AHI > 20 increases the risk of stroke to 4:33 times (95% confidence interval, 1:32 to 14:24, p = 0.02) compared with patients with AHI <5 where the hazard ratio 3.8 times higher (95% confidence interval, 0.74-12.81, p = 0.12). In conclusion it is stated that the apnea is severe to moderate risk of stroke increases from 30% to 90%, independent of other risk factors. Mansukhani et al. (20) in a prospective study in 174 patients with IS, communicated mortality of 11 (6.3%) in the first month and increased mortality in the group with apnea (relative risk, 5.3; 95% confidence interval, 1.4-2.1) compared with group without apnea. Good et al. (21) in a study of 47 patients with IS and apnea communicated mortality of 3 (6.4%) in the first month, and 10.6% after one year. Yaggi (22) in a study among 1022 patients, 697 (68%) had OSA. The OSA

syndrome was associated with stroke or death from any cause (hazard ratio, 2.24; 95 percent confidence interval, 1.30 to 3.86; p=0.004). After adjustment for age, sex, race, smoking, alcohol-consumption, body-mass index, and the presence or absence of diabetes mellitus, hyperlipidemia, atrial fibrillation, and hypertension, the OSA retained a statistically significant association with stroke or death (hazard ratio, 1.97; 95 percent confidence interval, 1.12 to 3.48; p=0.01). In conclusion he stated that the OSA significantly increases the risk of stroke or death from any cause, and the increase is independent of other risk factors, including hypertension.

Majority (51/87.9%) of 58 patients with apnea who survived had lesions at two or more locations (Table 3).

Otherwise, 12 (100%) patients out of 12 without apnea who survived had lesion in frontal lobe. Survival of patients with/without apnea is not statistically different in order to location of lesion (p>0.05) (Table 4).

Pašić (10) in a study done in our Klinik also has not found a link between the localization of stroke and SA (p = 0.58). Bassetti et al. (20) 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 also can not found a connection between respiratory problems in sleeping and localisation of

Survival rate (months)	With apnea left, right both (n=26) (n=44) (n=40)						Without apnea left right both (n=32) (n=28) (n=50)					
	N	%	N	%	N	%	N	%	N	%	N	%
1	25	96.2	43	97.7	40	100.0	32	100.0	28	100.0	50	100.0
2	25	96.2	42	95.5	38	95.0	30	93.6	28	100.0	50	100.0
3	25	96.2	42	95.5	37	92.5	30	93.6	28	100.0	49	98.0
4	25	96.2	41	93.2	37	92.5	30	93.6	27	96.4	49	98.0
5	25	96.2	41	93.2	37	92.5	30	93.6	27	96.4	49	98.0
6	25	96.2	40	90.9	35	87.5	30	93.6	27	96.4	49	98.0
7	25	96.2	39	88.6	35	87.5	30	93.6	27	96.4	49	98.0
8	25	96.2	37	84.1	34	85.0	30	93.6	27	96.4	49	98.0
9	25	96.2	37	84.1	34	85.0	30	93.6	27	96.4	49	98.0
10	25	96.2	37	84.1	34	85.0	30	93.6	27	96.4	48	96.0
11	25	96.2	36	81.8	33	82.5	30	93.6	26	92.6	48	96.0
12	23	88.5	36	81.8	32	80.0	30	93.6	26	92.6	48	96.0

**Table 5.** One-year survival rate after stroke with/ without sleep apnea according to the side of lesion.  $X^2=4.37$ ,  $p=0.11$  With apnea  $X^2=2.22$ ,  $p=0.33$  Without apnea

stroke. Parra et al. (23) in a study conducted on 161 patients with stroke and SA also can not find a link between SA and topographic location neurological lesions. Łabuz-Roszak et al. (24) in their study conducted on 27 patients with stroke (mean age: 66 +/- 10 years, BMI 24.4 +/- 4.4) are apnea at (15/59%) patients. There were no statistically significant differences that would indicate a connection between SA and stroke localization. Concerning the side of stroke 23 (85.5%) patients with SA who survived had lesion(s) in left hemisphere but this difference is not significant ( $X^2=4.37$ ,  $p=0.11$ ). Patients without SA 48 (96%) had lesion(s) at both sides but this difference is not significant ( $X^2=2.22$ ,  $p=0.33$ )(Table 5).

Wierzbick et al. (25) in their study analyzed 43 patients with stroke and SA are not verified significant correlation between the apnea and side of stroke. Pašić (10) in a study conducted on 200 patients with stroke and SA also can not find significant correlation between the apnea and side of stroke (left 33%; right 39.5%, both 27%) ( $X^2=1.98$ ,  $p=0.161$ ).

## 5. CONCLUSION

Survival of patients without sleep apnea in ischemic stroke is significantly better than in patients with apnea. Survival in patients with/without apnea in hemorrhagic stroke has no statistical difference. Localization and side of lesion do not have influence on survival.

**CONFLICT OF INTEREST: NONE DECLARED.**

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