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Med Arh. 2015 Jun; 69(3): 149-152
Received: April 05th 2015 | Accepted: May 25th 2015

Published online: 10/06/2015 Published print: 06/2015

One Year Outcome of Acute Stroke Patients with Sleep Apnea

Biljana Kojic, Adnan Burina, Osman Sinanovic

Department of Neurology, University Clinical Center Tuzla,
Medical School, University of Tuzla, Tuzla, Bosnia and Herzegovina

Corresponding author: Biljana Kojic, MD, PhD. Department of Neurology, University Clinical Center Tuzla . E-mail: biljana.kojic1@gmail.com

ABSTRACT

The aim of this study was to analyze one year outcome of the acute stroke patients with sleep apnea in order to gender and age. **Methods:** It was analyzed 110 patients with acute stroke and sleep apnea. Among them 65(59%) were men. Average age of all participant was 65.13±9.27 years. The same number and gender distribution of participants with stroke and without apnea were in control group. Evaluation of sleep apnea has been done with: "The Sleep Disorders Questionnaire," "Berlin Questionnaire to identify patients at risk for the sleep apnea syndrome" and "The Epworth Sleepiness Scale." **Results:** One year after stroke onset survived 91 (82.7%) out of 110 patients with apnea. Average age of survived patients was 63.66±8.78 years. Among them 52(80%) were men. In control group, without apnea survived 104 (94.5%) patients with average age of 65.00±8.62 years. Among them 62 (95.4%) were men. In men with apnea there is significantly lower survival range in order to patients without apnea ($X^2=8.22$, $p=0.004$). In women there is no difference. Survival of both gender in patients with apnea (22; 64.7%) was the lowest in group older than 70 years of age. Sex ratio (men : women) was 15 (68.2%):7(58.3%). Survival in both gender in patients without apnea was the same in group older than 70 years of age: 27 (81.2%) out of 33. Average age of patients who died with apnea was significantly higher in order to patients without ($t=1.97$, $p=0.03$). **Conclusion:** One year after stroke, significantly more patients survived without (94.5%) than with apnea (82.7%) ($p=0.01$). In order to sex survived range was significantly ($p=0.004$) lower in men with apnea than without but in women there is no difference. Survival range of both gender in patients with apnea was the lowest in group older than 70 years ($p=0.03$).

Key words: apnea, stroke, one year outcome, sex, age.

1. INTRODUCTION

Apnea 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 older than 40's. In the adults, obstructive sleep apnea (OSA) is much more often in comparison to the central sleep apnea (CSA) (84% vs. 0.4%). This is due to the concentric collapse of the oropharynx and hypopharynx, and the inability of the air to flow through these anatomical structures. CSA is a consequence of lesions in the medullary respiratory centers. Mixed sleep apnea (MSA) is a combination of two forms and occurs in 15% of all population (1). In women, incidence increases after menopause. In women who use hormonal therapy frequency of apnea is similar to period before menopause. SA prevalence among men 30 to 60 years of age is 10-20% (2). SA syndrome is described as an isolated risk factor for stroke or recurrent stroke which could be cause of death. They are independent to other cardiovascular and cerebrovascular risk factors. Hemodynamic, metabolic and hematological changes associated

with breathing disorders during sleep lead to decreased cerebral perfusion and increased coagulability which might be in pathophysiological background of the stroke and death (3). In the United States (U.S.), at least 5% of the general population has OSA. It is a risk factor for the development of arterial hypertension and coronary heart disease, and can lead to congestive heart failure and acute ischaemic stroke (4, 5). SA is found in 50-70% of patients with stroke (6).

2. THE AIM

The aim of this study was to analyze one year survival range of the acute stroke patients with sleep apnea in order to sex and age.

3. PATIENTS AND METHODS

It was analyzed 110 patients with verified SA in acute stroke (AS), treated at Department of Neurology, University Clinical Center Tuzla in the period December 2009 thorough may 2010. Acute stroke has been diagnosed

either by computerized tomography (CT) or magnetic resonance imaging (MRI) of the brain. Average age was 65.13±9.27 years. Among them it was 65 (59%) men. Number of patients with no apnea in control group was the same as well as gender ratio, with average age of 64±8.69 years. There was no significant difference in patient's age with or without SA neither in men nor women. 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, X² test, Arcus Quickstat Biomedical statistical program, as well as Long rank test with p<0.05 considered significant.

4. RESULTS

It was analyzed 110 patients with verified SA in acute stroke (AS), treated at Department of Neurology, University Clinical Center Tuzla in the period December 2009 thorough may 2010. Acute stroke has been diagnosed either by computerized tomography (CT) or magnetic resonance imaging (MRI) of the brain. Average age was 65.13±9.27 years. Among them it was 65 (59%) men. Number of patients with no apnea in control group was the same as well as gender ratio, with average age of 64±8.69 years. There was no significant difference in patient's age with or without SA neither in men nor women. 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, X² test, Arcus Quickstat Biomedical statistical program, as well as Long rank test with p<0.05 considered significant.

One year after a stroke in the group with SA survived significantly less patients in order to patients without SA (91/82.7% vs. 104/94.5%, X² = 7.49, p = 0.01). The average age of patients which survived with SA was 63.6±8.7 and 65.0±8.62 without SA. The maximum number of deaths was in a group of patients with SA and it was in second (4/21.1% died of 19 patients) and eleventh month (3/15.8% died of 19) after AS. Otherwise, patients without SA died in the second month (2/33.3% died of 6 patients) after AS (Table 1).

Sleep apnea is separated risk factor which correlates with bad outcome and increase long-term mortality in patients with stroke (10). Jaggi et al.

Outcome/ months with/ without apnea	with apnea N (110) %	without apnea N (110) %
1	109 99.1	110 100.0
2	105 95.5	108 98.2
3	104 94.5	107 97.3
4	103 93.6	106 96.4
5	103 93.6	106 96.4
6	100 91.0	106 96.4
7	99 90.0	106 96.4
8	97 88.2	106 96.4
9	97 88.2	106 96.4
10	97 88.2	105 95.5
11	94 85.5	104 94.5
12	91 82.7	104 94.5

Table 1. One-year outcome in patients with/without sleep apnea (11) in their study suggest that patients with SA and AS have a higher risk of mortality in stroke (HR 1.97, 95% CI 1:12 to 3:48) than in patients without SA. Kolominsky and Heuschmann (12) in a prospective study of 345 patients with first stroke ever, report their mortality from 28.5% in the first three months and 37% within the first year, which is higher than in our study. Slightly lower results than ours stated Rola et al. (13) in their study of 91 patients with stroke or TIA who have been followed-up for two years. SA was noticed in 61 (67.7%) patients with stroke or TIA. The rate of recurrent stroke or TIA was significantly higher in the group with SA 12 (19.7%, p<0.05) compared to group without SA 3 (10%). Mortality rates were not significantly different in patients with and without SA (4/6.6% and 2/6.7%). In a study of 161 patients with a first ever stroke (n=122) and TIA (n=39), 116 (71.4%) had AHI>10, and 45 (28%) had AHI>30. Mortality after two years was 22 (13.7%) which is somewhat lower than in our study (14). Good et al. (15) in a study of 47 patients with stroke and SA stated that after three months 3 died (6.4%), and after a year 5 (10.6%) patients. Dyken et al. (16) during the four years of monitoring patients with sleep apnea and MU found mortality of 21%. In study of Shahar et al. (17) the rate of survival of patients with SA

Outcome months	Men with apnea N (65) %	Men without apnea N (65) %	Women with apnea N (45) %	Women without apnea N (45) %	Total with apnea N (110) %	Total without apnea N (110) %
1	64 98.5	65 100.0	45 100.0	45 100.0	109 99.1	110 100.0
2	62 95.4	64 98.5	43 95.5	44 97.8	105 95.5	108 98.2
3	62 95.4	64 98.5	42 93.3	43 95.6	104 94.5	107 97.3
4	61 93.8	63 96.9	42 93.3	43 95.6	103 93.6	106 96.4
5	61 93.8	63 96.9	42 93.3	43 95.6	103 93.6	106 96.4
6	59 90.8	63 96.9	41 91.1	43 95.6	100 91.0	106 96.4
7	58 89.2	63 96.9	41 91.1	43 95.6	99 90.0	106 96.4
8	56 86.2	63 96.9	41 91.1	43 95.6	97 88.2	106 96.4
9	56 86.2	63 96.9	41 91.1	43 95.6	97 88.2	106 96.4
10	56 86.2	63 96.9	41 91.1	42 93.3	97 88.2	105 95.5
11	54 83.1	62 95.4	40 88.9	42 93.3	94 85.5	104 94.5
12	52 80.0	62 95.4	39 86.7	42 93.3	91 82.7	104 94.5

Table2. One-year outcome in patients with/without sleep apnea in order to sex men with/without * X2=8.22, p=0.004 women with/without X2=0.49, p=0.48

is significantly lower than in the patients without SA. Increased risk of stroke was higher for 60% in patients with SA compared to those without SA. One year after stroke survived significantly fewer male patients with SA than without (52/80% versus 62/95.4%, $X^2=8.22$, $p=0.004$). In women, the difference was not statistically significant (39/86.7% versus 42/93.3%, $X^2=0.49$, $p=0.48$) (Table 2).

5. DISCUSSION

Redline et al. (18) report 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%. Redline et al. (19) found SA and stroke in 72.2% men and 27.8% women. Increased risk of stroke in men with SA is the same like risk for stroke in men the years older. There is no statistical difference in the age of the men and women with SA ($t=-1.65$, $p=0.12$) who died. The average age of died men without SA was 57.67 ± 9.81 (range 41-85) years and women 70.00 ± 9.16 (range 41-85). No statistically significant differences in age of survivors as well as died patients without SA ($t=0.318$, $p=0.751$). Analyzing the age of patients who died with and without SA, it was found that the average age of death with SA was significantly higher than the age of patients without SA ($t=1.97$, $p=0.03$ —one-sided test). Significantly fewer survivors with SA was in the age group over 70 years (64.7% vs. 94.5%, $p=0.01$) than without SA (Table 3 and 4).

Similar results in terms of mortality distributed by age found in a study by Ancoli-Israel et al. (20) who evaluated 426 patients with stroke and SA in the period between 1981 and 1986 (mean age 72.5 years). Survival of patients with $AHI \geq 30$ was significantly shorten ($p=0.0034$), and an age was the strongest mortality predictor. Cardiovascular and pulmonary diseases are listed as independent risk factors for mortality. Young et al. (21) in their study, and lead to SA in the elderly is between 20%-50%, and the prevalence of SA increased with age. Patients with 70 years of age have nearly doubled percentage of SA in population with 40 years of age. Janssens et al. (22) stated that SA is associated with increased mortality in the elderly and patients with stroke and SA have a worse prognosis after three months as well as one year after stroke. Minoguchi et al. (23) stated that SA is an independent predictor of increased risk of stroke and mortality in elderly patients. Punjabi et al. (24) in a group of 1047 patients with stroke (587 men and 460 women), which have been followed in period of 8.2 years, found increased mortality in patients with sleep apnea. The hazard ratio for mild sleep apnea was 0.93 (95% CI: 0.80-1.08), moderate 1.17 (95% CI: 0.97-1.42) and severe 1:46 (95% CI: 1.14-1.86). Increased mortality was observed in patients with OSA, but the effect

Outcome/ months with apnea	Age 41-50 N (4) %	Age 51-60 N (28) %	Age 61-70 N (44) %	Age >70 N (34) %	Total N (110) %					
1	4	100.0	27	96.4	44	100.0	45	100.0	109	99.1
2	4	100.0	27	96.4	44	100.0	44	97.8	105	95.5
3	4	100.0	27	96.4	44	100.0	43	95.6	104	94.5
4	4	100.0	27	96.4	44	100.0	43	95.6	103	93.6
5	4	100.0	27	96.4	44	100.0	43	95.6	103	93.6
6	4	100.0	26	92.6	42	95.5	43	95.6	100	91.0
7	4	100.0	26	92.6	42	95.5	43	95.6	99	90.0
8	4	100.0	26	92.6	41	93.2	43	95.6	97	88.2
9	4	100.0	26	92.6	41	93.2	43	95.6	97	88.2
10	4	100.0	26	92.6	41	93.2	42	93.3	97	88.2
11	4	100.0	26	92.6	39	88.6	42	93.3	94	85.5
12	4	100.0	26	92.6	39	88.6	42	93.3	91	82.7

Table 3. One-year outcome in patients with sleep apnea in order to age

Outcome/ months without apnea	Age 41-50 N (5) %	Age 51-60 N (27) %	Age 61-70 N (45) %	Age >70 N (33) %	Total N (110) %					
1	4	100.0	27	100.0	45	100.0	33	100.0	110	100.0
2	4	100.0	27	100.0	45	100.0	31	93.9	108	98.2
3	4	100.0	27	100.0	45	100.0	30	91.0	107	97.3
4	4	100.0	27	100.0	45	100.0	29	87.9	106	96.4
5	4	100.0	27	100.0	45	100.0	29	87.9	106	96.4
6	4	100.0	27	100.0	45	100.0	29	87.9	106	96.4
7	4	100.0	27	100.0	45	100.0	29	87.9	106	96.4
8	4	100.0	27	100.0	45	100.0	29	87.9	106	96.4
9	4	100.0	27	100.0	45	100.0	29	87.9	106	96.4
10	4	100.0	27	100.0	45	100.0	28	84.8	105	95.5
11	4	100.0	27	100.0	45	100.0	27	81.2	104	94.5
12	4	100.0	27	100.0	45	100.0	27	81.2	104	94.5

Table 4. One-year outcome in patients without sleep apnea in order to age

is primarily seen in men younger than 70 years. Women and men older than 70 years had an increased mortality. Janssens et al. (22) suggest that OSA is associated with increased mortality in the elderly and patients with stroke and OSA have a worse prognosis after third and twelfth months after AS, and increased mortality.

6. CONCLUSION

One year after stroke, significantly more patients survived without (94.5%) than with apnea (82.7%) ($p=0.01$). In order to sex survived range was significantly ($p=0.004$) lower in men with apnea than without but in women there is no difference. Survival range of both gender in patients with apnea was the lowest in group older than 70 years ($p=0.03$).

CONFLICTS OF INTEREST: NONE DECLARED.

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