COGNITIVE FUNCTIONALITY OF PATIENTS WITH DELIRIUM AFTER STROKE

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SUMMARY

Background: Delirium is a syndrome that occurs in all age groups and in many clinical departments, and is most common in intensive care units. It is an emergency, in the overlapping fields of somatic medicine, neurology and psychiatry. Delirium occurs suddenly, dramatically, and requires a quick reaction, recognition and treatment. There are only a small number of studies that have reported delirium after a stroke. In our study, the goal was to determine the cognitive functionality of patients with delirium after a stroke.

Subjects and methods: This is a prospective study in which a group of 100 delirium patients in the acute phase of a stroke were evaluated for cognitive function. The control group consisted of the same number of patients with acute stroke who were not diagnosed with delirium. Neurological, neuropsychiatric and neuropsychological tests were performed in all patients at five different time periods. In these time periods, all patients were evaluated: Glasgow Coma Scale; Delirium Assessment Scale; The American National Institutes of Health Scale Assessment; Information-Memory-Concentration test; Dementia Score; Mini-Mental Test. The findings of computed tomography of the brain and magnetic resonance imaging of the brain were interpreted by a radiologist who was not familiar with the goals of this study.

Results: Cognitive functioning of delirious patients is statistically significantly worse after three and six months, and one year from stroke compared to those without delirium. There is no statistically significant difference in cognitive functioning between delirious patients in relation to gender, age, location and type of stroke and patients without delirium throughout one year from stroke. There is no significant difference in cognitive functioning between delirious patients during one year from stroke in relation to severity and type of delirium, and statistically significantly higher degree of cognitive dysfunction has those older than ≥65 years.

Conclusions: Delirium significantly reduces the cognitive functioning of patients after a stroke.

Key words: stroke - delirium - dementia

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INTRODUCTION

Organic psychiatric syndromes can be acute (delirium) or chronic (dementia). The risk of developing dementia after delirium in people over 65 is about 60% with an annual incidence of 18.1%. (Pavlović 2008). According to the World Health Organization (WHO) stroke is defined as the sudden development of focal or global symptoms and signs of cerebral dysfunction that last longer than 24 hours or lead to death, and are the result of a pathological process of vascular origin (Thorvaldsen et al. 1995). The basic division of stroke, according to the type of pathological process, is into ischemic stroke (IS) which covers 70-85%, and hemorrhagic stroke (HS). Stroke leads to focal or multifocal neuropsychological disorders. As a consequence of stroke, different degrees of impairment of physical, cognitive and psychosocial functioning lag behind (Demarin et al. 2003).

According to the definition from the International Classification of Diseases and Related Health Problems - 10th revision from 1994 (ICD-10) delirium not caused by alcohol or other psychoactive substances is an etiologically nonspecific organic cerebral syndrome characterized by simultaneous disturbance of consciousness and attention, perception, thinking, psychomotor beha-

vior, feelings of sleep rhythm and wakefulness. The most significant feature of delirium is a disorder of consciousness accompanied by a change in cognition that cannot be better explained by preexisting or developed dementia (Anonymous 1994). Delirium is one of the most common complications in the elderly during hospitalization and occurs in about 30% of such patients. It is a severe, multi-factor neuropsychiatric disorder with well-defined predisposing and precipitating factors. It is characterized by impaired consciousness and attention and development over a short period of time (Anonymous 2006, Siddiqi et al. 2006, Young et al. 2007). Stroke is a known risk factor for the development of delirium (Ferro et al. 2002).

The Mini-Mental State Exam (MMSE) is the most commonly used test for cognitive impairment in clinical practice (Folstein et al. 1975). However, MMSE is not designed to distinguish between delirium and dementia, and patients who are positive for cognitive impairment with MMSE require further evaluation. The two most commonly used assessment scales for the diagnosis of delirium are the Confusion Assessment Method-CAM (Inouye et al. 1990) and the Delirium Rating Scale (DRS) (Trzepacz 1988).

Vascular dementia (VaD) is acquired decline of cognitive, emotional skills and/or personality disorder cau-

sed by vascular factors, expressed enough to interfere with daily functioning and quality of life (Konno et al. 1997). VaD is the second most common cause of dementia with a frequency of 15% to 25% according to data obtained from autopsy and epidemiological studies (Stevens et al. 2002). Cognitive changes occur abruptly or gradually within three months of stroke or independently. Clinical features that raise suspicion of VaD are difficulty walking, falls, frequent urination, changes in personality and mood, psychomotor retardation, and dissective syndrome. In the neurological finding, there are focal signs such as hemiparesis, sensory and cranial nerve loss by central type, visual field defects, pseudobulbar syndrome, extrapyramidal signs, depression, mood swings and other mental disorders (Roman et al. 1993). For the diagnosis of VaD, it is necessary to determine that dementia and cerebrovascular disease coexist and to prove their causal relationship. The absence of cerebrovascular changes on visualization methods speaks against the diagnosis of VaD (Konno et al. 1997). There are only a small number of studies that have reported delirium after a stroke. The aim of our study was to determine the cognitive status of patients with delirium after stroke.

SUBJECTS AND METHODS

Participants

This is a prospective study conducted at the Clinic of Neurology of the University Clinical Center in Tuzla. The examined group of 100 delirious patients in the acute phase of stroke was evaluated for cognitive functioning. The control group consisted of the same number of patients with acute stroke who were not diagnosed with delirium. Both groups were matched according to gender, age, location of stroke, type, and severity of stroke.

The study group included patients who met the following criteria: confirmation of the diagnosis of ischemic stroke or hemorrhagic stroke by computed tomography (CT) and / or magnetic resonance imaging (MR) of the brain; neuropsychiatric assessment of delirium performed within seven days after stroke; Glasgow Coma Scale (GCS) > 8; written consent for participation in the research by the patient or a member of the patient's immediate family.

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 verified previous dementia/cognitive impairment (based on heteroanamnestic data from patient relatives, data from previous medical findings and based on the Dementia Score Test), patients with verified alcohol abuse (defined by at least 5 drinks per day), patients with previously verified mood disorders (if the patient has been treated for mood disorders at least once in their life, if they have been

prescribed medications for this disorder and if he has used them for more than a month), patients who have previously taken medications that could cause delirium.

Neurological, neuropsychiatric and neuropsychological tests were performed in all patients at five different time periods:

- First test - in the acute phase of stroke (first week of stroke).
- Second testing - upon discharge or one month after discharge from the Clinic (if the duration of delirium was shorter than the length of hospitalization, it was verified at discharge, and if the patient was discharged with milder symptoms of delirium, then those patients were tested even one month after discharge).
- Third test - three months after stroke.
- Fourth testing - six months after stroke.
- Fifth test - twelve months after stroke.

Measures/Instruments

In the stated time periods, all patients were evaluated:
- Glasgow Coma Scale (Teasdale & Jannett 1974) (in the first and second tests);
- Delirium Rating Scale-R-98 (Trzepacz 1999) (in all tests);
- American National Institute of Health Scale Assessment Scale (NIHSS) (Lyden et al. 2003) (in all tests);
- Information-Memory-Concentration test (Blased et. al. 1968) (in the third, fourth and fifth tests);
- Dementia Score (Hachinski et al. 1975) (in the first, third, fourth and fifth test);
- Mini-Mental State (Folstein et al. 1975) (in the third, fourth and fifth tests).

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 best motor response. These three scores were added together and the resulting sum represented the Glasgow Coma Scale which 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;
- mild lesion - if the score is 13 to 15.

Delirium Rating Scale-R-98

The Delirium Rating Scale-R-98 (DRS-R-98) is a thirteen-part observation scale: "Sleep-wake rhythm rhythm" (part 1), "Perception and hallucinations disorders" (part 2), "Imagination" (part 3), "Excitement" part 4), "Language" (part 5), "Disorders of the thought

process" (part 6), "Anxiety" (part 7), "Motor braking" (part 8), "Orientation" (part 9), "Concentration" (part 10), "Short-term memory" (part 11), "Long-term memory" (part 12), "Possibility of spatial orientation" (part 13). In addition to these 13 items, three other diagnostic items were used to help distinguish delirium from other disorders: chronological onset of symptoms, symptom variability, and physical disorders. Based on the sum of the first 13 items, the degree of severity of delirium was obtained.

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 the 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.

Information-Memory-Concentration test

This test is part of the Blessed Dementia Scale (Blassed et al. 1968). It consists of questions that assess mental status, divided into three scales. These are the Information Scale, the Memory Scale and the Concentration Scale. The maximum scores on these three scales are 15, 16 and 6. Cognition preservation has a score of 0, and the maximum disorder has a score of 37.

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 11 questions that examine 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:

- score <10 severe dementia,
- score 10-20 moderate dementia,
- score 21-25 mild dementia,
- score 26 borderline score according to dementia and
- score 27-30 no dementia.

Dementia Assessment Scale

One of the more commonly used versions of the Dementia Score is the version made by Hachinski and co-workers in 1975. The maximum score is 28 and indicates the highest degree of dementia. A score less than 4 is considered normal, 4-9 is a mild disorder, and 10 or more is moderate to severe. Score values may indicate the degree of dementia progression during repeated examinations.

Determination of delirium symptoms was performed by the Delirium Assessment Scale-R-98 (DRS-R-98) (Trzepacz, 1999) and delirium criteria according to the fourth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) (Anonymous, 1994). Delirium was diagnosed in those patients who had more than 16 points on DRS-R-98 and who met the criteria for delirium according to DSM-IV. Patients with a score of 16-32 are marked as a milder form, and those over 32 as a more severe form of delirium.

The criteria of the American "National Institute for Neurological Disorders and Cerebrovascular Insult" and the European "International Association for Research and Education in Neuroscience" (NINDS-AIREN) (Roman et al., 1993) were used to confirm the diagnosis of VaD.

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;
- lesion size;
- silent heart attacks.

Brain MRI was performed in patients with a clinical picture of a brainstem lesion, with a negative CT scan of the brain, or when the finding needed to be supplemented with an MRI scan. Strokes, by type, are divided into: (a) hemorrhagic and b) ischemic strokes. If the CT or MR finding failed to show an acute, silent or old brain lesion, then its localization was determined on the basis of a neurological examination and grouped into insults in the region:

- - brain stem / cerebellum and
- - hemisphere (left, right).

Based on the localization changes verified by the findings of CT and MR of the brain, ischemic strokes are grouped into strokes in the region:

- brain stem / cerebellum,
- brain stem / cerebellum + hemisphere and
- hemisphere (left, right, bilateral).

Lesions in the hemispheres were grouped into superficial (anterior and posterior circulation) and deep (lacunar infarction, striato-capsular, thalamus). According to the CT and MR findings of the brain, hemorrhagic stroke was grouped according to the same principle as for ischemic stroke with the addition of intraventricular hemorrhage. The research included the registration of the following socio-demographic characteristics: gender and age. A hyperactive variant of delirium was considered if the patient showed mild, moderate, or severe anxiety in part 7 of DRS-R-98. A hypoactive variant was diagnosed if in part 8 the patient showed a slight, moderate or severe slowing of spontaneous movements.

The degree of neurological deficit was evaluated on the day of admission to the recent National Institute of Health Stroke Scale (NIHSS) (Lyden et al. 2001).

Statistical Analyzes

Numerical test results were statistically processed, analyzed and compared, in order to obtain answers to questions formulated within the research objectives. The obtained data were grouped, coded and entered into a specially created database. During the entry, additional validation (logical control) of the collected data was performed. 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. Testing of each variable for belonging to the normal distribution was performed, using the Kolmogorov-Smirnoff test, and a histogram. To assess the statistical significance of the differences in the obtained results, the following were used: Hi-square test. All statistical tests were performed with a level of statistical probability of 95% ($p<0.05$). Statistical processing was performed with the program SPSS ver. 17.0 (Chicago, IL, USA).

The research was approved by the Ethics Committee of the University Clinical Center Tuzla.

RESULTS

All patients on admission had an „IMC score" of 0 (preservation of cognition) and a normal score according to the "Dementia Assessment Scale". There was a statistically significant higher incidence of delirious patients with impaired cognitive functioning after three ($p=0.0005$, Yatess correction = 42.1, df = 1), six months ($p=0.0005$, Yatess correction = 39.8, df = 1) and one year ($p=0.0005$, Yatess correction = 37.7, df = 1) from MU (Table 1).

Delirious patients had statistically considerable higher cognitive impairment according to the Dementia Rating Scale after three months ($p=0.0005$, Pearson Chi-Square = 51.3, df=2), six months ($p=0.0005$, Pearson Chi-Square = 54.0). , df=2) and one year ($p=0.0005$, Pearson Chi-Square = 49.4, df = 2) from the onset of stroke (Table 2).

Delirious patients had statistically significantly poorer cognitive functioning according to the „MMS score" after three months ($p=0.0005$, Pearson Chi-Square = 43.9, df = 3), six months ($p=0.0005$, Pearson Chi-Square = 74.7, df = 4) and one year ($p=0.0005$, Pearson Chi-Square = 55.0, df = 3) from the onset of stroke in relation to patients without delirium (Table 3).

There was no statistically significant difference in the score of the "IMC test" between patients with delirium and without delirium in relation to gender, age, location and type of stroke after one year from its occurrence ($p>0.05$). In relation to the score of the "Dementia Assessment Scale" between patients with delirium and without delirium, there was no statistically significant difference in relation to gender, location and type of stroke after one year.

Patients with delirium ≥65 years of age had a higher incidence of cognitive impairment as measured by the Dementia Rating Scale compared to patients without delirium of the same age group after one year of stroke ($p=0.0005$, Pearson Chi-square = 7.3, df = 2) (Table 4).

Table 1. Incidence of patients with cognitive impairment one year after stroke

IMC score	Cognitive functioning						p*-value
	With delirium		No delirium		Total		
	N	%	N	%	N	%	
							0.0005
Preserved cognition	20	11.7	72	42.1	92	53.8	
Impaired cognition	55	32.2	24	14.0	79	46.2	
Total	75	43.9	96	56.1	171	100.0	

* Chi-square test;   IMC score- Information-Memory-Concentration test

Table 2. Degree of cognitive impairment according to the "Dementia Assessment Scale" one year after stroke

Dementia score	Cognitive functioning						p*-value
	With delirium		No delirium		Total		
	N	%	N	%	N	%	
							0.0005
Normal (score 0-3)	18	10.7	73	43.2	91	53.8	
Mild disorder (score 4-9)	39	23.1	20	11.8	59	34.9	
Moderate to severe disorder (score 10-28)	17	10.1	2	1.2	19	11.2	
Total	74	43.8	95	56.2	169	100.0	

* Chi-square test

Table 3. Degree of impairment of cognitive functioning according to the MMS score one year after stroke

MMS-score	Cognitive functioning						p*-value
	With delirium		No delirium		Total		
	N	%	N	%	N	%	
							0.0005
Severe dementia	14	8.3	1	0.6	15	8.9	
Moderate dementia	10	5.9	2	1.2	12	7.1	
Mild dementia	33	19.5	18	10.7	51	30.2	
Without	17	10.1	74	43.8	91	53.8	
Total	74	43.8	95	56.2	169	100.0	

* Chi-square test; MMS-score - Mini-Mental State Score

Table 4. Incidence of patients ≥65 years of age with cognitive impairment one year after stroke

Dementia score	Cognitive functioning						p*-value
	With delirium		No delirium		Total		
	N	%	N	%	N	%	
							0.0005
Normal (score 0-3)	11	9.9	50	45.0	61	54.9	
Mild (score 4-9)	24	21.6	9	8.1	33	29.7	
Serious (score 10-28)	16	14.4	1	0.9	17	15.3	
Total	51	45.9	60	54.1	111	100.0	

* Chi-square test

Table 5. Frequency of cognitive impairment in delirious patients after one year in relation to age

Dementia score	Cognitive functioning of delirious patients						p*-value
	≤64 yeras		≥65 years		Total		
	N	%	N	%	N	%	
							0.04
Normal (score 0-3)	7	9.5	11	14.9	18	24.3	
Mild (score 4-9)	15	20.3	24	32.4	39	52.7	
Serious (score 10-28)	1	1.4	16	21.6	17	23.0	
Total	23	31.1	51	68.9	74	100.0	

* Chi-square test

There was no statistically significant difference in the „IMC score" between delirium patients in relation to severity and type of delirium (p>0.05). After one year of stroke, delirious patients ≥ 65 years of age had a statistically significantly higher degree of cognitive impairment as measured by the Dementia Assessment Scale compared to delirious patients aged ≤ 64 years (p=0.04, Pearson Chi-square = 6.5, df = 2) (Table 5).

DISCUSSION

In institutions where patients with delirium are diagnosed, there are about 40% of patients who have dementia, 30% mild cognitive deficit and 14% who have depression. We should be aware that the basis of a large number of cases of delirium is dementia, and its etiological clarification is necessary. We talk about VaD when the patient has memory problems, concentration disorders and disturbances in everyday life that limit certain previously common activities, and are primarily caused by vascular disease. This form of the disease most often occurs in the elderly, hence in a population with many patients with one or more different risk factors for cerebrovascular diseases, such as diabetes, hyperlipidemia, unregulated or poorly regulated high blood pressure, previously suffered from stroke, narrowing of the carotid arteries as the main blood vessels supplying to the brain. These include certain heart diseases, such as past heart attacks or heart rhythm disorders, which are one of the common causes of recurrent stroke (Pavlović 2008).

Vascular dementia will occur in a patient who has had stroke on several occasions. It will also occur in patients who have suffered more extensive stroke with the manifestation of motor disorders, hemiparesis, hemiplegia, speech disorders, but the same often occurs in patients who do not even know that they have had stroke. The accumulated brain damage in these patients ultimately leads to the discomfort that the patient brings to the physician, and a brain imaging (CT or MRI) reveals the nature of the brain damage. In contrast to Alzheimer's type dementia, the problems with the vascular

form of dementia occur more abruptly, often seemingly from a period of normal cognitive functioning.

Patients with delirium stroke have a longer hospital stay and an increased incidence of vascular dementia (Gustafson et al. 1991, Henon et al. 1999). The association of delirium with dementia is seen in 8% to 43% depending on the examined population (Bucht et al. 1999). The risk of developing dementia after delirium in the elderly over the age of 65 is about 60% with an annual incidence of 18.1% (Rockwod et al. 1999).

Moroney et al. (1996) in their prospective study reported that the incidence of dementia was doubled in patients with stroke compared to those without stroke. Although there were a small number of patients with dementia in both groups, it can still be concluded that stroke as a brain perfusion impairment may contribute to the development of pathogenetic mechanisms for the development of dementia. They also noticed that older patients have an increased risk of developing dementia.

Delirium in patients with stroke is associated with a poorer functional but not vital prognosis at discharge and after six months. In about 20% of patients, after the cessation of acute confusion, residues can be identified up to 6 months later (Hill et al. 1992). These are most often various cognitive deficits. These disorders can be an introduction to the onset of dementia. It is likely that the critical factor is the remaining cognitive reserve.

Bilateral lesions, involvement of the frontal and limbic areas, as well as temporal and parietal regions are considered important (Erkinjuntti et al. 1999). Most patients with infarcts larger than 40 milliliters have global dementia, but many with smaller infarcts even have volumes below 15 milliliters (Esiri et al. 1997).

Rockwod et al. (1999) evaluated 203 patients with stroke in their study. Their mean age was ≥65 years and 38 patients with delirium (22 with delirium and dementia and 16 with delirium) and 158 without delirium and dementia were observed for three years (median 32.5 months). The incidence of dementia for patients without delirium was 5.6% per year and 18.1% for patients with delirium. The risk of developing dementia after delirium in the elderly over the age of 65 is about 60%.

As independent factors in the development of dementia after stroke, the following were found: infarct characteristics, degree of white matter change, atrophy of the medial or central temporal lobe and lower education (Pohjasvaara et al. 2000). People who develop dementia have larger infarcts, increased number of infarcts, larger right-sided changes, larger infarcts in "strategic" positions in the left hemisphere (thalamo-cortical connections, putamen, globe palidus and deep areas in the posterior cerebral artery basin), micro-vascular changes, diffuse white lesions masses, bilateral infarcts, and the simultaneous neurodegenerative process (Ballard et al. 2000, Pohjasvaara et al. 2000).

Witlox et al. (2010) in their meta-analysis presented the association of delirium in the elderly with poor outcome. Studies on elderly subjects with delirium and data on the development of dementia after a minimum observation of three months were observed. In addition to the increased risk of death, delirious patients also had an increased risk of institutionalization and development of dementia.

Melkas et al. (2011) found that post-stroke delirium occurs in 19% of patients, and low levels of education, pre-existing cognitive impairment, severe stroke, and severe post-stroke disability (Rankin score between 3 and 5) are the most significant risk factors for post-stroke delirium. They found that delirium after stroke was also associated with the appearance of VaD after 3 months.

This study found that there was a significantly higher incidence of delirious patients with impaired cognitive function measured by the "IMC test" after three months (p=0.0005), six months (p=0.0005) and one year (p=0.0005) than stroke. Delirious patients also had significantly greater impairment of cognitive functioning according to the "Dementia Assessment Scale" after three months (p=0.0005), six months (p=0.0005) and one year (p=0.0005) from stroke. They also had significantly poorer cognitive functioning according to the „MMS score" after three months (p=0.0005), six months (p=0.0005) and one year (p=0.0005) from stroke.

There was no statistically significant difference in the score of the "IMC test" between patients with and without delirium in relation to gender, age, location and type of stroke after one year from its occurrence (p>0.05). In relation to the score of the "Dementia Assessment Scale" according to gender, localization and type of stroke, there was no significant difference after a year, as well as between delirious patients in relation to severity and type of delirium (p> 0.05).

Patients with delirium ≥65 years of age had a higher incidence of cognitive impairment as measured by the Dementia Assessment Scale compared to patients without delirium of the same age group after one year from stroke (p=0.03). There was no significant difference in the „IMC-score" between delirium patients in relation to severity and type of delirium (p>0.05).

After one year from having a stroke, delirium patients ≥65 years of age had a significantly higher degree of cognitive impairment measured according to the "Dementia Assessment Scale" compared to delirious patients aged ≤64 years (p=0.04). The results of a significantly higher degree of cognitive impairment in patients with delirium after stroke are similar to the results of previous research on this issue and based on that it can be concluded that delirium is a significant risk factor for the development of VaD.

It is not possible to restore the lost nerve cells in the brain to the patient with any known treatment, but we can help him control the values of blood pressure, fat and blood sugar. We can stop smoking, reduce alcohol use, treat heart and carotid artery disease. In this way, the possibility of new incidents in the blood vessels of the brain is reduced, thus slowing down the progression of dementia. Comprehensive and conscientious health care, which includes both physical and mental activity, is most important in preventing many diseases, including dementia.

CONCLUSIONS

Delirium significantly reduces the cognitive functioning of patients after a stroke. Cognitive functioning of delirious patients is statistically significantly worse after three and six months, and one year from stroke compared to those without delirium. There is no statistically significant difference in cognitive functioning between delirious patients in relation to gender, age, location and type of stroke. and patients without delirium for one year from stroke. There is no significant difference in cognitive functioning between delirium patients during one year of stroke in relation to severity and type of delirium, and statistically those that are older than ≥65 years have higher degree of cognitive dysfunction.

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