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NEUROLOGIC DEFICIT AND LEVEL OFCONSCIOUSNESS IN PATIENTS AFTER STROKE: CORRELATION WITH RISK FACTORS

Aleksandra Angelova[1], Glorija Gashpar[2], Anita Arsovska[3]
[1]University Clinic for Neurology, Clinical Center "Mother Theresa", Skopje, R.North Macedonia
[2]PHI Specialized Hospital for Geriatric and Palliative Medicine "13th November", Bitola, R.North Macedonia, [3]University Clinic for Neurology, Faculty of Medicine ,Ss Cyril and Methodius University in Skopje, R. North Macedonia

Abstract

Stroke remains the second leading cause of death and the leading cause of disability worldwide, with its incidence and mortality differing between countries. Even though there has been a substantial decrease in the burden of stroke in high-income countries, around 70% of stroke cases occur in low or middle-income countries, with great negative effect on the system.

Although risk factors are well known, it is still unclear to which extent each of them impacts the neurologic deficit and the level of consciousness of the patient.

The aim of this study is to identify the influence of 6 common stroke risk factors - hypertension, atrial fibrillation, cardiomyopathy, diabetes mellitus, previous stroke or transient ischemic attack and dyslipidemia on the neurologic deficit quantified by National Institutes of Health Stroke Scale and the level of consciousness quantified by Glasgow Coma Scale.

For this purpose, existing records of 157 patients from October 2019 to October 2020 were analysed.

The study showed that atrial fibrillation (p=0.048), cardiomyopathy (p=0.024) and previous stroke or transient ischemic attack (p=0.03) significantly influence the mean National Institutes of Health Stroke Scale score, while atrial fibrillation (p=0.0067) and dyslipidemia (p=0.029) significantly influenced mean Glasgow Coma Scale scores.

This emphasizes the need of proper management of risk factors, especially higlighting stroke prevention in atrial fibrillation.

Keywords: stroke, risk factors, neurologic deficit, level of consciousness

Introduction

Stroke remains second leading cause of mortality (2019) and most common cause of dissability worldwide, and eventhough incidence and mortality related to stroke substantially decrease in high income countries, this disease still has a strong negative effect on the health system in low and middle income countries.

This has been shown by the fact that around 70% of strokes, 87% of deaths related to stroke, and the total number of disability adjusted life years – happen in these countries.

They also have higher percentage of haemmorhagic strokes and the average age of patients is lower than those in high income countries (Fernado Lanas et al. The Lancet journals, 2021[1].

Stroke related incidence and mortality differ between countries, geographical regions, and ethnic groups, thus to have a better managment of this problem it is essential for middle or low income countries such as North Macedonia, to recognize the local incidence and prevalence of stroke and stroke related risk factors, and the importance of their relationship.

The Global Burden of Disease Study points out that 90.5% of global burden of stroke was due to modifiable risk factors, while Feigin et al proposed that more than 90% of stroke related burden on the health system is due to these factors.

Most common stroke risk factors are hypertension, diabetes mellitus, heart diseases as coronary arthery disease, cardiomiopathy, heart failure and atrial fibrillation, personal or family history of stroke or transient ischemic attack (TIA) [1].

Stroke presents an acute condition which is mainly caused by other systematic vascular or heart condition, like atherosclerosis, hypertenson and cardial embolism.

Seventy-five percent of the patients have comorbid heart disorders such as hypertension and coronary arthery disease, while others have comorbid heart conditions that cause cardiac embolism like atrial fibrillation, cardiomiopathy, acute myocardial infarction and endocarditis [1].

Prevalence of chronic diseases is rising worldwide, partly due to better treatment of acute conditions and also in proportion with better life expectancy.

There is a well defined correlation between age and comorbidities, therefore patients with stroke, especially ischaemic, often have more than 1 comorbidity. Rigler et al. noted that only 6 % of the patients with ischaemic stroke don't have any comorbidities, while 40% of them have more than 3 comorbidities. [2]

Therefore at this moment, there are many people in the world living with several chronic conditions, and they have worse outcome regarding their overall health and the managment of diseases is more complex.

Multimorbidity defined as having ≥2 assosiated long-term diseases, in patients with stroke is asossiated with greater mortality in short and long term.

There is also limited evidence suggesting that multimorbidity in stroke patients is associated with greater stroke severity, lower baseline functional status, longer rehabilitation time, poorer functional gain, lower overall functional status following rehabilitation, longer hospital stays, increased readmission rates, and higher overall health care utilization in the longer term which is associated with increased economic costs [1].[3]

Eventhough the number of preexisting comorbidities increased mortality, it is still unclear how each comorbidity affects stroke severity.

The aim of this study is to identify the most common comorbidities in stroke patients and to analyse their predictive value and impact on the neurological deficit – quantified with National Institutes of Health Stroke Scale (NIHSS) which is the most frequently used clinical tool for neurological deficit and stroke severity assesment, and has predictive properties regarding stroke outcome, but also to evaluate their impact on the level of consciousness – quantified by Glasgow Coma Scale (GSC), universal clinical tool used to objectively measure depth and extent of consciousness impairment in all types of acute brain injury, with powerfull predictive value for stroke outcome.

Materials and methods

Existing records of 157 patients were analysed, in 1 year period 01.10.2019-01.10.2020. Patients were admited to the University Clinic of Neurology in Skopje, North Macedonia - department of Urgent Neurology and were diagnosed with stroke (ischemic and haemmorhagic) confirmed by CT scan.

Inclusion criteria were patients in all age groups with signs of acute cerebral infarction on CT scan, with the following preexisting comorbidities: hypertension (HTA), atrial fibrillation (AF), cardiomyopathy (CMP), diabetes mellitus (DM), prior stroke or transientischemic attack (TIA) and hyperlipidemia (HLP).

The exclusion criteria were patients with no signs of recent stroke on CT scan, patients without complete medical history or patients that were transferred to other facility. Overall, 88 people were discharged from the hospital, and 69 had lethal outcome. In the analysis we included other parameters such as neurologic deficit quantified by NIHSS score in 2 time periods: on admission (or in the first 24 hours) and on discharge (except for patients with lethal outcome).

Depending on the score we divided stroke patients in 5 categories: no signs of stroke (0 points), minor stroke (1-4 points), moderate stroke (5-15 points), moderate to severe stroke (16-20 points) and severe stroke (21-42 points).

We also included level of consciousness in stroke patients quantified by GSC score, calculated in 2 time periods: on admission and on discharge (except patients with lethal outcome), and based on this score we dividedpatients according to level of consciousness and brain injury in 3 groups: mild injury (15-13 points), moderate injury (12-9points) and severe injury (8-3 points).
Results from Get with the Guidelines – Stroke in North America [2], show that stroke severity based on NIHSS score is a strong predictor for stroke outcome alongside comorbidity index, and they suggested this score to be calculated as soon as possible after admission in hospital.

Gennarelli et al. demonstrated a continuous, progressive assosiation between increased mortality after any brain injury and decreases of GSC score from 15 to 3[6].

Statistical analysis

The statistical analysis of patients data in this study was provided by the statistical programe SPSS 23,0. Shapiro Wilk's testwas used to test the normality of data distribution.

Categorical (atributive) variables are shown with absolute and relative numbers. Numerical (quantitive) variables are shown with mean and standard deviation.

For comparison of the scores on admission and discharge, we used “Student t-test, for dependent samples” and “Wilcoxon matcher pairs test”, and for comparing scores of patients with or without risk factors we used Student t-test for independent samples.

Correlation between number of risk factors with both scales was analysed with Spearman's rank correlation coefficient.

Statistical significance was defined at level p<0.05. Data of interest is shown in tables and graphics

Results

There were 175 participants in this study, all admitted at the department of Urgent Neurology, University Clinic of Neurology, with diagnosis of stroke (ischemic or haemorrhagic), aged from 29-91 years, with mean age 68.2 ± 12.3 years. Of them, 53.5% (84 patients) were male, and 46.5% (73 patients) were female.

According to the obtained score from NIHSS on admission and discharge, the severity of neurological deficit was statistically significantly different at discharge (p<0.0001). Mild symptoms of stroke had 6.4% (10 patients) on admission, 32.95% (29 patients) on discharge; severe neurologic deficit had 36.9% (58 patients) on admission, while on discharge only 4.5% (4 patients) had severe neurological deficit. (table 1)

Statistically significant difference on discharge compared to admission, was confirmed also for level of consciousness (p<0.0001). Mild impairment od consciousness had 46.5% (73 patients) on admission, 85.2% (75 patients) on discharge; while severe impairment of consciousness had 28% (44 patients) on admission, and only 2.3% (2 patients) on discharge. (table 1)

Table 1. Number of patientsdistributed in five stroke severity categories according to NIHSS score and three categories according to GSC score on admission and discharge

	admission	**discharge**	**p-value**
NIHSS			
No signs of stroke n (%)	1 (0.64)	5 (5.68)	Z=5.5 p<0.0001sig
Mild stroke n (%)	10 (6.37)	29 (32.95)	
Moderate stroke n (%)	63 (40.13)	41 (46.59)	
Moderate to severe stroke n (%)	25 (15.92)	9 (10.23)	
Severe stroke n (%)	58 (36.94)	4 (4.54)	
Total	157	88	
GSC			
Mild impairment of consciousness n (%)	73 (46.50)	75 (85.23)	Z=6.1 p<0.0001sig
Moderate impairment of consciousness n (%)	40 (25.48)	11 (12.5)	
Severe impairment of consciousness n (%)	44 (28.02)	2 (2.27)	
Total	157	88	

Z(Wilcoxon matched pairs test)

Mean NIHSS score was 17.8±5.6 on admission, and significantlly lower at discharge with mean value 8.1±3.2 (p<0.0001). (picture 1)

At p<0.0001, we confirmed significantlly higher mean GSC score on discharge compared to mean GSC score on admission (10.6±4.1 versus 14.1±1.7). (picture 2)

Fig.1. Mean NIHSS score on admission and discharge

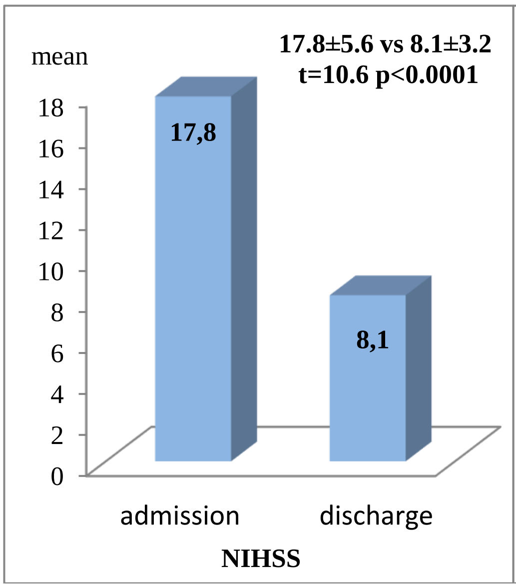
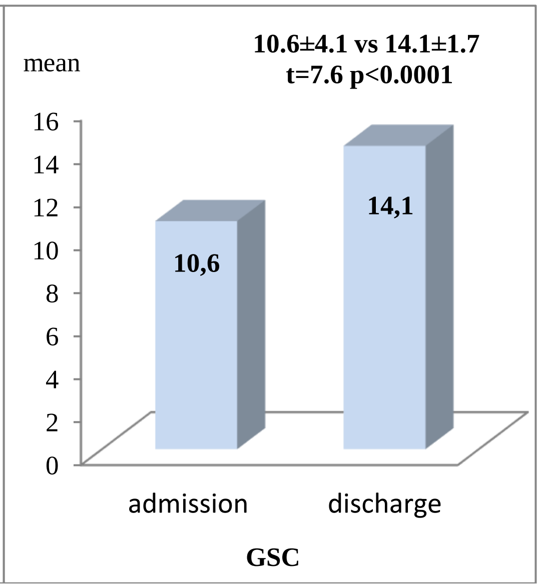


Fig. 2. Mean GSC score on admission and discharge



t(Student t-test)

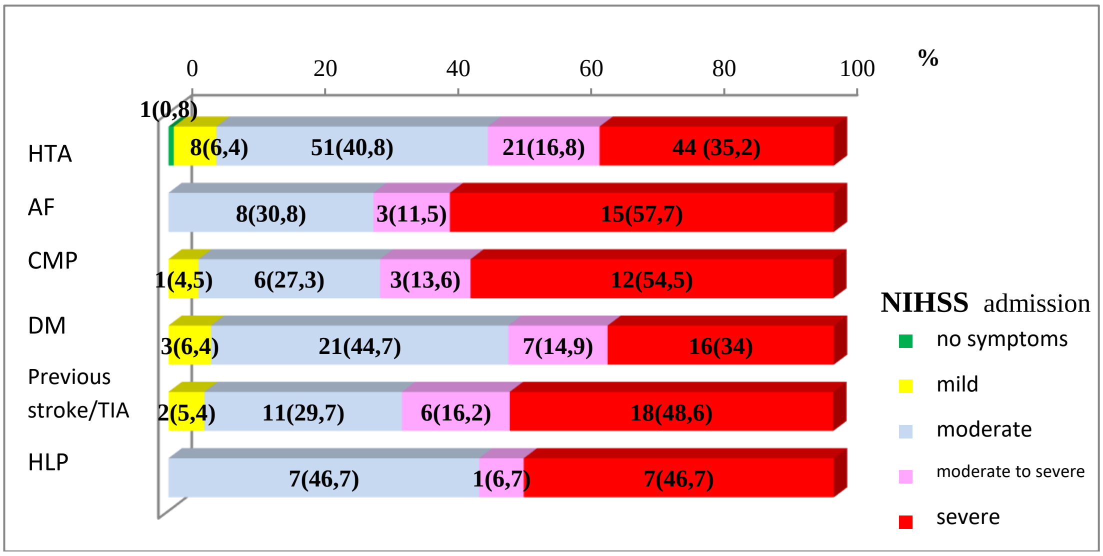
In this contingent, 13%(21) of the patients did not have positive history for any of the analysed risk factors. Regarding the analysed risk factors, hypertension was dominant at 79.6% (125 patients), while regarding the number of present risk factors, most of the patients had 2 risk factors – 35% (55 patients),(table 2)

Table 2. Distribution of risk factors and number of risk factors in 157 stroke patients

Risk factors	**n (%)**
Hypertension (HTA)	125 (79.62)
Atrial fibrillation (AF)	26 (16.56)
Cardiomyopathy (CMP)	22 (14.01)
Diabetes mellitus (DM)	47 (29.94)
Previous stroke or transient ischemic attack (TIA)	37 (23.57)
Hyperlipidemia (HLP)	15 (9.55)
Number of risk factors	
0	21 (13.38)
1	47 (29.94)
2	55 (35.03)
3	23 (14.65)
4	9 (5.73)
5	2 (1.27)

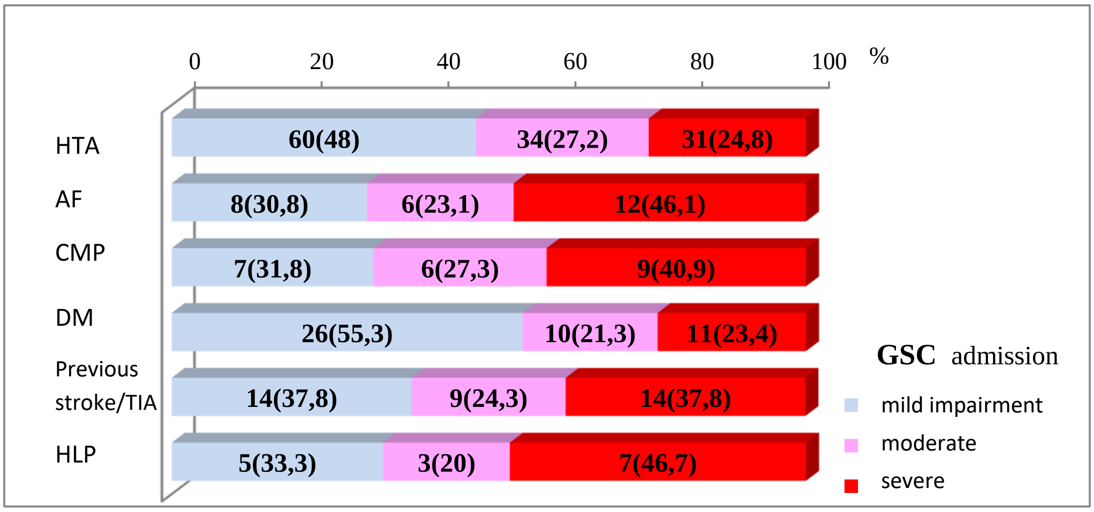
Distribution of patients with hypertension, atrial fibrillation, cardiomyopathy, diabetes mellitus, prior stroke or transient ischaemic attack and hyperlipidemia, regarding severity of neuorlogic deficit quantified by NIHSS, showed that severe neurologic deficit had 35.2% (44/125 patients) with hypertension, 57.7% (15/26) patients with atrial fibrillation, 54.55% (12/22 patients) with cardiomyopathy, 34% (16/47 patients) with diabetes mellitus, 48.65% (18/37 patients) with previous stroke or transient ishemic attack and 46.7%(7/15 patients) with hyperlipidemia (picture 3).

Fig.3. Distribution of patients with examined risk factors according to NIHSS score on admission in five categories



Severe impairment of consciousness was found in 24.8% (31/125 patients) with hypertension, 46.15% (12/26 patients) with atrial fibrillation, 40.9% (9/22 patients) with cardiomyopathy, 23.4% (11/47 patients) with diabetes mellitus, 37.8% (14/37 patients) with prior stroke or transient ischemic attack and 46.7% (7/15 patients) with hyperlipidemia. (picure 4)

Fig. 4. Distribution of patients with examined risk factors according to GSC score on admission in three categories



Mean NIHSS score had no significant difference between patients with or without hypertension (p=0.15), with or without diabetes melitus (p=0.45), with or withot hyperlipidemia (p=0.15),while it was significantly different between patients with or without atrial fibrillation (p=0.048), with or without cardiomiopathy (p=0.024), and between patients with or without previous stroke or TIA (p=0.03).

Mean NIHSS score was significantly higher in patients with atrial fibrillation compared to patients without heart rhythm disorders (21.23 ± 10.5versus17.14 ± 9.3), in patients with cardiomyopathy compared to patients without cardiomiopathy (22.09 ± 9.9versus17.12 ± 9.4), as well as in patients with previous stroke or TIA compared to those without this condition (20.81 ± 10.03versus16.90 ± 9.3).

Comparisson for mean GCS was statistically insignifficant between patients with or without hypertension (p=0.1), with or without diabetes mellitus (p=0.29), with or without prior stroke or TIA (p=0.074), and it was statistically significant between patients with or without atrial fibrillation, as a result of substantially lower mean GSC score in the group of patients with atrial fibrillation (8.61 ± 4.2± 10.5versus10.98 ± 3.9;p=0.0067), as well as in patients with or without hyperlipidemia, as a result of substentially lower mean GSC score in the group of patients with hyperlipidemia (8.40 ± 4.9versus 10.82 ± 3.96;p=0.029).

Borderline significance was noted for cardiomiopaty, with lower mean GSC score for patients with cardiomyopathy compared to patients without cardiomyopathy (9.04 ± 4.5 versus 10.84 ± 3.9). (table 3)

Table 3. Relationship between examined risk factors and mean NIHSS and GCS scores on admission and its significance.

Variable		**NIHSS I** mean ± SD	**p-level**	**GSC I** mean ± SD	**p-level**
HTA	yes	17.26 ± 9.4	t=1.4	10.86 ± 3.9	t=1.65
	no	20.0 ± 10.2	p=0.15 ns	9.53 ± 4.7	p=0.1 ns
AF	yes	21.23 ± 10.5	t=1.99	8.61 ± 4.2	t=2.75
	no	17.14 ± 9.3	*p=0.048sig	10.98 ± 3.9	**p=0.0067 sig
CMP	yes	22.09 ± 9.9	t=2.27	9.04 ± 4.5	t=1.92
	no	17.12 ± 9.4	*p=0.024 sig	10.84 ± 3.9	p=0.056 ns
DM2	yes	16.94 ± 9.6	t=0.75	11.13 ± 3.98	t=1.07
	no	18.20 ± 9.6	p=0.45 ns	10.36 ± 4.1	p=0.29 ns
Prior stroke or TIA	yes	20.81 ± 10.03	t=2.18	9.54 ± 4.8	t=1.8
	no	16.90 ± 9.3	*p=0.03 sig	10.92 ± 3.8	p=0.074 ns
HLP	yes	21.20 ± 11.1	t=1.4	8.40 ± 4.9	t=2.2
	no	17.46 ± 9.4	p=0.15 ns	10.82 ± 3.96	*p=0.029 sig

t(Student t-test) *p<0.05;**p<0.01

Results from this study showed that patients with 3 or 4 risk factors had higher mean **NIHSS score(**20.7±11.1 and 23.0±8.4, accordingly), and lower mean **GSC score(**9.8±4.9and8.4±4.2, accordingly) compared to patients with 1 or 2 risk factors, but without confirmed statistical significance (p>0.05). (table 4)

Table 4. Relationship between number of risk factors and mean NIHSS and GSC score on admission and its significance.

Number of risk factors	n	**NIHSS I** mean ± SD		**GSC I** mean ± SD	**p-level**
0	21	18.9±10.0	F=2.1 p=0.085 ns	10.0±4.6	F=1.8 p=0.12 ns
1	47	15.4±8.5		11.7 ±3.4	
2	55	17.4±9.4		10.6±3.9	
3	23	20.7±11.1		9.8±4.9	
4	9	23.0±8.4		8.4±4.2	
5	2	6.0; 32		3;14	

F(Analisys of variance)

Analysed correlation between number of risk factors and scores obtained by NIHSS and GSC scales, showed positive, direct correlation (R=0.124) between number of risk factors and NIHSS, while between number of risk factors and GSC there is a negative, indirect correlation (R=-0.122).

With the increase of stroke risk factors, we noted higher NIHSS score and lower GCS score. These two correlations did not confirm statistical significance (0.12 and 0.13 accordingly). (table 5, picture 5 and 6)

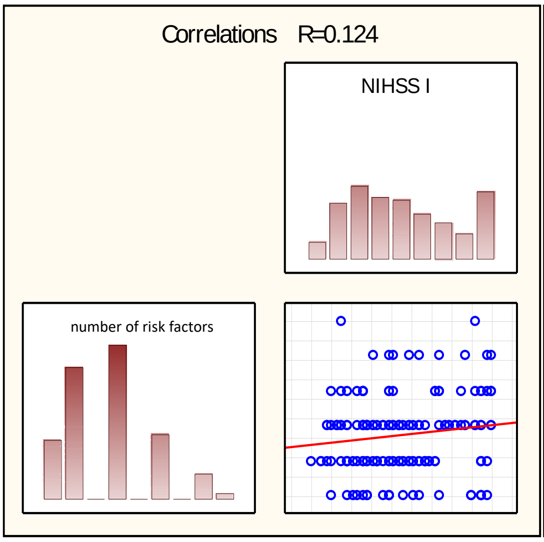
Table 5. Correlation between number of stroke risk factors and NIHSS and GSC score.

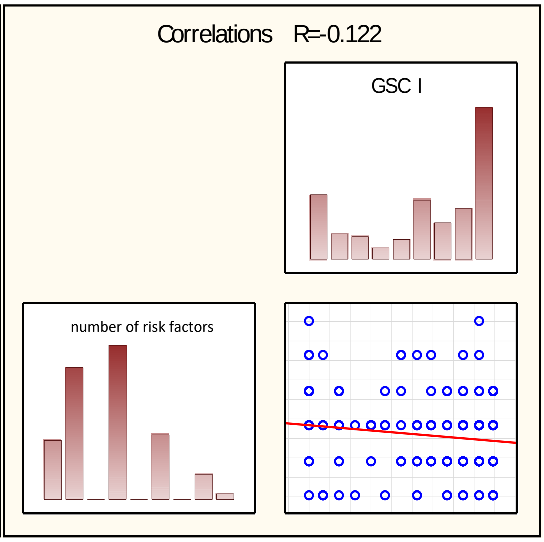
CORRELATION		
Number of stroke risk factors	**R**	**p-level**
NIHSS I	0.124	0.12 ns
GSC I	-0.122	0.13 ns

R(Spearman rank order correlation)

Fig.5 Correlation between number of stroke risk factors and mean NIHSS score on admission.

Fig.6 Correlation between number of stroke risk factors and mean GCS score on admission.





Discussion

In our study 6 stroke risk factors were analysed: hypertension, atrial fibrillation, diabetes mellitus, cardiomyopathy, previous stroke or transient ischemic attact, and hyperlipidemia.

Our goal was to describe their distribution in group of respondents and to evaluate their influence on stroke severity and consciousness. Study showed that few of them, including atrial fibrillation, cardiomyopathy and previous stroke or TIA have strong impact on stroke severity, while atrial fibrillation and hyperlipidemia were shown to have significant influence on the level of consciousness, and cardiomiopathy had border significance.

Hypertension was shown to be the most prevalent cardio-vascular risk factor in few other studies, which was the case in our study too, and was detected in 125 patients (79.6%).

This is in accordance with previous studies, like the one from Dušica Simić-Panić et al [3], conducted in hospital in Novi Sad, where 70-80% of the patients with ishcemic stroke had hypertension. There is a determined linear correlation between hypertension and risk for stroke.

In some prospective studies, each 10mm/Hg reduction of arterial tension was associated with 33% reduction of stroke risk as primary prevention [3].

Different mechanisms can explain the negative influence that hypertension has in cerebrovascular autoregulation, including the combination of changed mechanical characteristic in blood vessels induced by extensive remodelling and the effect it has on smooth muscles tonus in blood vessels which leads to increased wall thickness and wall-lumen ratio.

These changes in autroregulation can especially target and damage periventricular white matter which is located between different arterial territories and is therefore sensitive to hipoperfusion [4].

Besides this, these changes also contribute infarction volume and size after blood vessel obstruction. Results from our study showed that severe stroke and neurologic deficit had 35.2% (44/125 patients) with hypertension, while severe impairment od consciousness (GSC<3) had 24.8%(31/125 patients) patients with hypertension.

Mean NIHSS score was not significantly different between patients with or without hypertension (p=0.15) and also mean GSC score did not show signifficant difference between patients with or without hypertension (p=0.1).

In the study of Rasha H. Soliman et al [5], more stroke risk factors were correlated and analysed, hypertension was also the most prevalent risk factor and was detected in 62.3% of patients, and they also showed that mean NIHSS score was significantly higher in hypertensive patients (p=0.023).

We found an interesting information in Sthe study of Jie Li et al. [6] who found that increased arterial tension on admission in hospital in stroke patients had protective role against early consciousness disorder.

In the same study out of 569 respondents 456 had hypertension, 119 (59.8%) of them had early conscious disorder (somnolence, sopor, coma, confusion, dellirium), while 237 (64.1%) did not have early conscious disorder (p=0.137).

Another prospective study on a spanish cohort with acute stroke showed that increased or decreased blood pressure in the first 24 hours Is assosiated with early neurological deteoriration and bad prognosis.

Second analysed risk factor was atrial fibrillation, the most common heart rhythm disorder in the elderly assosiated with 4 to 5 times increased risk for stroke. In our study 26 patients (16.56%) had atrial fibrillation making it 4th most frequent comorbidity, with lower occurrence compared to 20.9% in Karatas et al [7] study,or 26.3% in Rasha H. Solman [10], study and 17.2% in the study of Saposnik et al. [8], with a note that in all of the previous, only patients with ischemic stroke were included.

Karatas et al found correlation between large cortical infarcts and atrial fibrillation and described that patients with this risk factor had worse functional outcome compared to patients with sinus rhythm. Etiology of stroke in patients with atrial fibrillation is most commonly cardioembolic and targets large cerebral blood vessels which results with severe stroke [9].

Few authors concluded that patients with atrial fibrilation have increased mortality in the first 30 days after stroke. Di Cralo et al. [15] in their study which consisted of 2740 patients noted positive correlation between atrial fibrilation and mortality, disability and hendicep.

In our study severe stroke and neurologic deficit quantified by NIHSS score had 57.7%(15/26 patients), while other patients with atrial fibrillation had moderately severe and moderate strokes, but none of them had mild to no symptoms at all. Regarding consciousness impairment 46.15% (12/26) patients with atrial fibrillation had severe consciousness impairment quantified with GSC score.

Mean NIHSS score was significantly higher in patients with atrial fibrillation compared to those without heart rhythm disorder (21.23 ± 10.5versus17.14 ± 9.3; p=0,048). Comparison of mean GSC was statistically significant between patients with or without atrial fibrillation, as a result of significantly lower mean GSC score in the group of patients with atrial fibrillation (8.61 ± 4.2± 10.5versus10.98 ± 3.9;p=0.0067).

Similar to our results, atrial fibrillation was shown to be independent risk factor for stroke severity and stroke related disability and had significant correlation to NIHSS (p<0.001), according to Kim K [10].

In Peter Appeleros et al. [11] study where few stroke risk factors were analysed, atrial fibrillation, dementia and age were included in the multivariate analysis for stroke severity because of significant positive assosiation in the univariate analysis (p<0.01 in the univariate model and p=0.01 in the multivariate model). Huey-Juan Lin et al. [12] also suggested that stroke severity is asossiated with atrial fibrillation and chances for stroke fatality are increased for these patients (p=0.048).

In Jie Li [11] study, early consciousness disorders in stroke patients were analysed, and it was shown that incidence of early consciosness impairment is the highest in patients with cardioembolic stroke, and smallest in patients with small arthery occlusion, making these results consistent with data obtained from another study suggesting that impaired consciousness is 3.2 more likely to occur in patients with cardioembolic infarcts compared to atherothrombotic infarcts. In this same study by Jie Li, out of 569 patients – 155 had atrial fibrillation and 85 (42.7%) had early consciousness disorder, while 70 (18.9%) did not have early consciousness disorder (p<0.001).

Additionally, Europian Community Stroke Projectreported that the incidence of coma and confusion in the first week after stroke is higher in patients that have atrial fibrillation [13].

Heart disorders and diseases are second most common cause of acute cerebrovascular event and are diagnosed in 1/3 of patients with stroke [14] , including atrial fibrillation which is the most important modifiable stroke risk factor and the reason for large cardio-embolic infarcts that present with severe neurological deficit and severe consciousness impairment.

But there are other heart conditions that are a potential sourse of embolism, as are dilated cardiomyopathy, hypertophic cardiomyopathy, heart valve diseases, left chamber hypertophy, atrial mixom and congenital heart diseases (PFO, atrial septal aneyrism, ventrical septal defects).

Cardiomyopathies are a heterogeneous group of conditions, associated with mechanical or electrical disfunction, caused by different reasons, sometimes genetic, and are often presented with hypertrophy or dilatation of the left ventricle.

Known complications of hypertophic cardiomyopaties are systematic embolisam and stroke, and are often seen in patients that have accompanying heart rhythm disorder.

In the study of Shintaro Haruki et al. [15] an incidence of 1% was reported for stroke and embolic events in a period of 1 year in a group of patients with hypertrophic cardiomyopathy, and half of the patients did not have previously diagnosed atrial fibrillation.

More advanced age and enlarged dimensions of the left chamber were associated with embolic events in patients with hypertrophic cardiomyopathy but without atrial fibrillation.

Dilated cardiomyopathy is also associated with increased risk for cerebral embolisam, with increased tendency for formation of thrombotic
masses as a consequence of slower blood flow through dilatated heart ventricles. According to the Framingham Heart Study, every 10mm enlargment of left atrium increases the risk of ischaemic stroke twice.

In our study 22/157 (14.01%) patients had diagnosis of cardiomyopathy, without mentioning the type. In the study of Dusica Simic Pancic et al[4] the prevalence of dilated cardiomyopathy was 9.9% and Atalay et al.[16] report a prevalence of 12.4%.

From the total number of patients with cardiomyopathy, in our study, 12/22 (54.55%) had severe neurological deficit, 3/22 had moderate to severe neurological deficit, 6/22 had moderate neurological deficit, 1/22 patient had mild neurological deficit, and none had no signs or symptoms. Regarding consciousness impairment, 9/22 (40.9%) patients had severe consciousness impairment, 6/22 (27.27%) had moderate consciousness imparement and 7/22 (31.82%) had mild consciousness impairment.

Mean NIHSS score was significantlly different between patients with or without cardiomyopathy ($p=0.024$), being significantly higher at patients with cardiomyopathy versus without (22.09 ± 9.9versus17.12 ± 9.4). On border of significance it was noted lower mean GSC score at patients with cardiomyopathy compared to those without cardiomiopathy (9.04 ± 4.5versus10.84 ± 3.9).

Diabetes mellitus and stroke are both vascular diseases. Diabetes causes disfunction and pathological remodelling of cerebral blood vessels, and ultimately influences brain injury in strokes and rehabilitation process afterwards. Diabetes mellitus significantly increases stroke risk, especially in younger individuals.

Incidence of diabetes in stroke patients dramatically increased from 1997 (20%) to 2006 (30%), while the combination of accompanying hypertension and diabetes is especially powerfull when it comes to increased stroke risk.

In contrast to large cerebral infarcts caused by embolisam in big cerebral blood vessels, infarcts in deep and small cerebral blood vessels (lacunar strokes) are associated with longterm hypertension and diabetes mellitus.

Besides hypertension, diabetes mellitus is considered to be the most important reason for diseases of small blood vessels, and has been identified as an independant variable for symptomatic recurrence in patients with first lacunar stroke.

Diabetes is also considered to increase stroke risk 2 to 6 times, while hyperglycaemia is an independent predictor for worse clinical outcome in stroke, although not all patients presenting with hyperglicemia on admission have diabetes mellitus.

Increased glycaemia leads to critical changes in neurovascular unit: there is deposition of extracellular matrix in the basal membraine of capilaries and penetrating arteriolles, leading to interuption of communication between blood vessels, astrocytes and neurons, and there is also endothelial dysfunction. It is considered that hyperglycaemia leads to neuronal death.

Level of glycaemia in diabetes is important factor for size of the infarct. Dyslipidemia, hypertension and obesity are atherogenic risk factors often occuring in patients with diabetes mellitus type 2 [17]. It is also considered that diabetes mellitus is an independant risk factor for stroke with aterothrombotic etiology.

The influence of diabetes mellitus is greater in female compared to male.

The combination of hypercholesterolemia and hypertension in patients with diabetes, increases risk of vascular damage. In our study 47/157 (29.94%) patients had diagnosis diabetes mellitus at admission, which is lower compared to 34.0% in Dusica Simic Pancic et al. [3] study. In the study of Di Carlo et al [15], 21.8% patients had diabetes mellitus, while in the study of Mizrahi et al.[18], 37.7% patients had diabetes mellitus, and Atalay et al. [22], reported occurance of 35.9%. In the study of Rasha H. Soliman et al.[10], diabetes mellitus was detected in 34.7% patients admitted to the University Hospital Beni Suef in Upper Egipt.

Out of the total number of patients with diabetes mellitus, in our study, 16/47 (34.04%) had severe neurological deficit and stroke, 7/47 (14.89%) had moderate to severe neurologic deficit and stroke, 21/47(44.68%) had moderate neurological deficit and stroke, 3/47 (6.38%) had mild neurological deficit and none of the patients had no signs or symptoms at all. Severe consciousness impairment had 11/47 (23.4%) patients with diabetes mellitus, moderate consciousness imapirment had 6/47 (21.21%) and mild consciousness impairment had 26/47 (55.32%).

Mean NIHSS score had no significant difference between patients with or without diabeltes mellitus (p=0.45), and mean NIHSS score for patients with diabetes was 16.94 ± 9.6. When compared mean GSC score did not differ significantly between patients with or without diabetes mellitus (p=0.29), and mean GSC score at admisson for diabetes patients was 11.13 ± 3.98.

In Rasha H Soliman's study mean NIHSS score for stroke patients with diabetes mellitus was 9.43 ± 5.18 (p=0.221), also mean NIHSS score had no significant difference between patients with or without diabetes mellitus. In Jie Li et al.[11] study where patients were investigated for early consciousness disorders (somnolence, sopor, coma, delirium and confusion) in a hospital in China, out of 569 patients, 146 had diabetes mellitus, 56 (28.1%) patients had early conscious disorder, and 90 (24.3%) patients did not have early consciousness disorder (p=0.320).

In the same study investigations showed that high glycaemia on admission, alongside higher NIHSS score on admission, massive infarct and history of alcoholism were all independent risk factors for early consciousness disorder.

These results were consistent with cross-sectional study of 9044 Caucasian patients, which showed that patients with abnormal GSC score are more probable to be male, elderly or with positive history for diabetes, alcoholism or previous stroke or TIA.

Besides this, authors suggest that poor glycaemia control is a predictor for early consciousness disorder in patients with diabetes mellitus and acute ischemic stroke, therefore history of diabetes mellitus was identified as independent predictor for early consciousness impairment in patients with acute ischemic stroke, but only when the model of multivariate logistic regression did not include serum glucose concentration on admission to hospital.

Authors of this study, suggest that these findings are a possible reflection of the fact that hyperglycemia increases coagulation and inhibits fibrinolysis, consequently decreasing reperfusion in ischemic tissue which then contributes to increased infarct volume. At the same time hyperglycemia inhibits vasodilatation, increases production of reactive oxygen and nicotin adenine dinucleotide phosphate.

Besides all this, hyperglycaemia is considered to inhibit mitochondrial function in the ischemic penumbra, causing additional intracellular acidosis.

Authors conclude that good monitoring and control of serum glucose in patients with diabetes mellitus and ischemic stroke – can decrease the rate of early consciousness disorder and improve prognosis.

Next we analysed previous stroke or transient ischemic attack (TIA). According to Werner Hacke et al. – history of previous stroke or transient ischemic attack is strong independent risk factor for mortality and systematic embolism/stroke.

Increased risk is more associated with previous stroke (with or without transient ischemic attack), while only history of transient ischemic attack is a weaker predictor.

Data from 2 population-based studies for transient ischemic attack in the United Kingdom, report an estimated risk for stroke after TIA from 8% to 9% in the first 7 days, and 12% in the first month. Another study investigated patients with TIA in the emergency department, concluding that they had estimated risk for strokeof 10.5% in the first 90 days, and 5.3% in the first 2 days after TIA [19].

In our study 37/157 (23.57%) patients had history of previous stroke, with or without sequelae and/or history of TIA. In most of these patients, modifiable risk factors had not been identified or managed properly, and they probably did not take medications properly. Severe neurological deficit had 18/37 (48.65%) patients, 6/37 (16.22%) had moderate to severe neurologic deficit, 11/37 (29.73%) had moderate neurologic deficit, 2/37 (3.41%) had mild neurologic deficit and none of them had no signs or symptoms of stroke at all.

Regarding consciousness impairment 14/37 (37.84%) patients had severe consciousness impairment, 9/37 (24.32%) had moderate impairment of consciousness and 14/37 (37.84%) patients had mild consciousness impairment.

Mean NIHSS score was significantly higher (p=0.03) in category of patients with prior stroke or TIA compared to those without (20.81 ± 10.03 versus 16.90 ± 9.3). Regarding impairment of consciousness, comparisson of mean GSC score was statistically insignificant between patients with or without history of previous stroke or TIA (p=0.074).

Compared to our results, in the study of Rasha H. Soliman [10] history of previous stroke or TIA were analysed separately, and in the same study history of previous stroke was registered in 27.5% of patients, which is higher compared to our study, while mean NIHSS score for patients with history of previous stroke compared to those without was statistically insignificant (p=0.316), with mean NIHSS score 10.67 ± 5.19 for patients with previous stroke and mean NIHSS 10.08 ± 6.06 for patients without previous stroke.

Also when history of TIA was analysed, there was not a significant difference between patients with positive history of TIA compared to those without positive history of TIA, p=0.725, (10.33 ± 4.39 versus 10.24 ± 5.91). Compared to Jie Li's study for early consciousness impairment in a chinese cohort of 569 patients, total number of 111 patients had history of previous stroke, 34/111 (17.1%) patients had early conscious impairment and 77/111 (20.8%) did not present with conscious impairment when admitted to the hospital (p=0.285 χ 2 test).

Dyslipidemia and hypercholesterolemia are known risk factors for many vascular diseases, including stroke, but there is complex correlation between cholecterol levels and lipid profile and the subtype of stroke, the strongest association existing with atherosclerotic subtypes of stroke.

There are many studies where different parameters of lipid profile and the risk of stroke were analysed, with strongest accent on total cholesterol and LDL cholesterol, but the results obtained were conflicting, probably as a consequence of the heterogenity of stroke subtypes.

The risk for stroke can be reduced in majority of patients with dyslipidemia and coronary arthery disease, diabetes, hypertension and the elderly with statins [19].

For every 1 mmol decrease of LDL cholesterol, there was 17% reduction of fatal and nonfatal strokes (Baigent et al.) [20].

In our study patients who had hyperlipidemia, without specification on parameters of lipid status, were total 15/157 (9.55%) which is substantially lower than the number of patients with hyperlipidemia in Rasha H. Soliman's study (58.1%), but also compared to Grau et al [21] study with 35.3%, and Jie Li study with 23.02%.

In our study 7/15 (46.7%) patients had severe neurological deficit, 1/15 had moderate to severe neurological deficit, 7/15 (46.7%) had moderate neurological deficit and none of them had mild to no signs and symptoms of stroke. Severe consciousness disorder had 7/15 (46.7%) patients, 3/15 (20%) had moderate consciousness impairment, and 5/15 (33.33%) had mild consciousness impairment.

Mean NIHSS score had no significant diference between patients with or without hyperlipidemia (p=0.15),(21.20 ± 11.1 versus 17.46 ± 9.4).

Reagarding consciousness impariment, comparisson of mean GSC was statisticaly significant (p=0.029) between patients with or without hyperlipidemia, as a result of significantlly lower mean GSC score for patients with hyperlipidemia (8.40 ± 4.9 versus10.82 ± 3.96;p=0.029).

Similarly in Rasha J. Soliman [10] study, mean NIHSS score had no significant difference between patients with ot without hyperlipidemia (p=0.834), with mean NIHSS of 10.33 ± 5.88 versus 10.13 ± 5.79.

In Lucas Restrepo et al's [22] study, analysed patients who received statins before stroke, had milder neurological deficit compared to patients who did not receive statins (NIHSS 15.5 ± 14 for patients who did not receive statins versus 9.5 ± 16 and 11 ± 18 for patients who received statins before stroke and patients who received statins pre and post stoke , accordingly. P=0.0871).

In Jie Li study 131 patients had hyperlipidemia, 34/131 (17.1%) patients had early consciousness disorder and 97/131 (26.2%) did not have early consciousness disorder (p=0.014). In conclusion, patients with early consciousness disorder had lower rate of hiperlipidemia, which is contrary to results obtained in our analysis.

We have finally analysed the correlation between number of comorbidities and mean NIHSS and GSC on admission.

Previous studies described the problem with multimorbidity in patients with stroke, with estimated prevalence of 43% to 94%.

Estimated prevalence of multimorbidity in stroke patients with 66+ years is almost 99% [5]. In our contingent, only 13.4% (21/157) patients did not have any comorbidity on addmision, while 86.6% (136/157) patients had at least one of the above mentioned six comorbidites. Only 1 risk factor had 29.94% (47/157) patients, 2 risk factors had 35.03% (55/157) patients, 3 risk factors had 14.65% (23/157) patients, 4 risk factors had 5.73% (9/157) patients, and 5 risk factors had 1.27% (2/157) patients.

Limited evidence note that multimorbidity in patients with stroke is associated with severe presentation on admission, severe neurologic deficit, lower functional status prior and post rehabilitation, longer hospital stays.

One study that analysed comorbidities for 18 years (1994-2011), showed that the proportion of patients who had stroke and at least one comorbidity has increased from 40.5% to 47.0% for ischemic strokes and from 32.0% to 44.7% for haemmhoragic strokes [23].

In Altafi et al's [24] study, there was no significant correlation between NIHSS score and risk factors.

Our study showed positive direct correlation between number of risk factors and NIHSS score (R=0.124), which means that when a patient has more risk factors NIHSS score is increased, while there is a negative indirect correlation between GSC score and number of risk factors (R=-0.122), meaning that a patient with more risk factors has lower GSC score on admission, but both correlations were statistically insignificant (0.12 and 0.13 accordingly).

Conclusion

According to our study, patients who had atrial fibrillation had significantly higher mean NIHSS score and significantly lower GSC score on admission, probably as a result of severe strokes caused by cardioembolisam in the major cerebral arteries.

Cardiomiopathy which also affects regular blood flow in the heart, and history of a previous stroke or TIA are other risk factors related to statistically significant higher mean NIHSS scores and severe neurological deficit on admission.

For level of consciousness, we found that besides atrial fibrillation, hyperlipidemia is a risk factor that significantly impacts mean GSC score. Suprisingly, Diabetes Mellitus did not significantlly impact mean NIHSS and GCS scores.

Taking into account these findings, it is essential to prevent strokes in patients with atrial fibrillation, with proper diagnosis, education and medical treatment.

Further investigations should include other prevalent comorbidities in patients with stroke, so we can provide proper primary prevention and decrease stroke occurence in our country.

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