### RESEARCH

### **Open Access**



# Relationship of Alberta Stroke Program Early CT Score (ASPECTS) with the outcome of ischemic stroke and the neurocognitive stroke biomarkers

Nehal Tharwat Mohammed El-Sayed<sup>2</sup>, Mohammed Abd Elsalam<sup>1</sup>, Mohamed E. Flifel<sup>1</sup> and Saad Shawki<sup>3</sup>

Ahmed Esmael<sup>1\*</sup>, Mohammed Elsherief<sup>1</sup>, Ahmed Abdel Khalek Abdel Razek<sup>2</sup>,

### Abstract

**Background:** Reliable and acceptable biomarkers are needed to anticipate the outcome and cognitive impairment following ischemic stroke. The goal of this research is to examine the association of ASPECTS with cognitive decline, biomarkers of stroke, and acute ischemic stroke outcomes. This study included 120 patients with ischemic stroke in the middle cerebral artery region. The initial NIHSS, non-contrast CT brain assessed by ASPECTS, and the biomarkers of cognitive decline such as ESR, CRP, S100B, MMP9, and glutamate were investigated. The Montreal Cognitive Assessment and modified Rankin scale (mRS) were evaluated after 3 months. Correlations between ASPECTS, MoCA, biomarkers of cognitive impairment, and mRS were done by Spearman correlation.

**Results:** The incidence of cognitive impairment in our patients was 25.8%. Stroke biomarkers (ESR, CRP, S100B, MMP9, and glutamate) were significantly increased in cognitively disabled individuals with significantly lower mean MoCA scores than in cognitively intact patients. There was a strong direct correlation linking the initial ASPECTS and total MoCA test score after 3 months follow-up. Cases with unfavorable outcomes were older, more incidence of hypertension, and had higher average initial NIHSS (P < 0.05). While the average ASPECTS scores for the favorable outcome group of patients were significantly higher and there was a significant negative correlation between the initial ASPECTS and modified Rankin Scale score.

**Conclusions:** ASPECTS is a reliable scale to identify the extent of acute ischemic injury and could participate in assessing the outcome. ASPECTS and particular neurocognitive stroke biomarkers will enable the early detection of post-stroke cognitive impairment.

Trial registration Registration of Clinical Trial Research: Clinical Trials.gov ID: NCT04235920

Keywords: Stroke, ASPECTS, mRS, NIHSS, MoCA, Neurocognitive stroke biomarkers

### Background

Strokes are known to be the third most frequent cause of death after cardiac and neoplastic disorders [1]. Moreover, stroke is a significant cause of mortality and morbidity all around the world. The effect of ischemic injury is so rapid because of the very few reserves of glucose inside the brain, the key energy material [2]. So far, the CT brain is considered to have been the examination of

\*Correspondence: deltaneuro@yahoo.com

<sup>1</sup> Neurology Department, Faculty of Medicine, Mansoura University, Mansoura 35516, Dakahlia, Egypt

Full list of author information is available at the end of the article



© The Author(s) 2021. **Open Access** This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit http://creativecommons.org/licenses/by/4.0/.

choice for diagnosing patients with acute ischemic stroke (AIS). With regard to adequate assessment in patients with acute ischemic stroke, brain CT is an easy, effective, appropriate and affordable tool [3]. The availability of the non-contrast CT brain to the initial evaluation makes it an effective neuroimaging marker to evaluate acute care outcomes [4, 5].

In order to assess the magnitude of early ischemic alterations in the brain, the Alberta Stroke Program Early Computed Tomography Score (ASPECTS) has been widely used [6], and was confirmed to anticipate neurological outcomes [7]. In specific, stroke cases with higher ASPECTS treated with thrombolytic therapy have better outcomes [8–10].

In AIS patients, the incidence of cognitive dysfunction is around 25% following 3 months of follow-up [11]. The measurement of cognitive functions by traditional neuropsychological methods after acute stroke is very controversial due to several factors that cause false interpretation of study results, such as the nature of medical status, apathy, depression, and anxiety disorders [12]. In order to predict the nature of its course and the effectiveness of treatment, reliable and acceptable biomarkers are therefore needed to anticipate the occurrence of poststroke cognitive impairment [13, 14]. The purpose of our research is to examine the association of ASPECTS with cognitive decline, biomarkers of stroke, and acute ischemic stroke outcomes.

#### Methods

#### Study design and participants

This research was a prospective cross-sectional study that included 120 patients presented with AIS referred to the neurology department in the time from October 2019 and March 2020. One hundred and twenty patients were involved in this research, diagnosed with the first occurrence of acute MCA territorial ischemic infarction during 2 days from the initial symptoms and signs. AIS was identified as a quickly evolving neurological dysfunction with a recognized apparent onset, and an early brain CT with no ICH evidence. The exclusion criteria included infarction of the anterior or posterior cerebral arteries, venous sinuses infarctions, or prior strokes. Also patients with severe dysphasia or aphasia were excluded.

#### On admission

#### **Clinical assessment**

A history of vascular risk factors for all cases had been collected. Full general and neurological studies were performed. To measure the intensity of the stroke and the initial morbidity, early GCS and NIHSS were estimated. NIHSS was categorized into three categories: mild (0–5), moderate (6–15), and extreme ( $\geq$  16) [15].

#### Neuroimaging evaluation

Every patient performs CT imaging by means of (16-Multi-slice GE, optima 520, China). For all cases, the initial non-contrast CT brain was performed after the onset and after 7 days. Images produced captured in the axial cut, 5-mm segments starting from the base up to the vertex, were used by all patients. The criteria for imaging were the following: 120 kVp, 320 mA, FOV of 195 mm, and table speed of 15 mm/rotation.

#### Laboratory investigations

Within 24 h of the onset of the stroke, blood samples were obtained for all patients. Basic laboratory tests such as full blood count, serum lipids, clotting pattern, liver and kidney functions, and fasting and postprandial glucose levels were performed. Also, biomarkers of cognitive decline such as ESR, S100B, MMP9, CRP and glutamate were assessed.

#### Image analysis

Image review was carried out by two neuroradiologists separately for evaluation of CT brain. For all patients, ASPECTS scoring was determined. CT brain images were analyzed for markings of parenchymal hypoattenuation, lack of grey and white matter distinction, and obscure sulci. ASPECTS offers accurate techniques for ischemic stroke assessment by using the "M1, M2, M3, M4, M5, M6, I: insula, IC: internal capsule, L: lentiform, and C: caudate" ten-point score, all representing one point (Fig. 1). A score of ten indicates a CT scan that is normal. To every affected region of the CT brain, one point is reduced. Therefore, a value of 0 indicates extensive ischemia in the MCA area [16].

#### Functional outcome in cases of stroke

In the following 3 months, functional outcome of stroke in each patient was assessed by the modified Rankin Scale. MRS is a widely used scale to assess impairment which can be used in patients with stroke as a prognostic tool and graded into seven outcomes ranging from no symptoms (0 scores) up to death (6 scores) [17].

#### Assessment of cognition

Montreal Cognitive Assessment (MoCA) Arabic form was utilized for the evaluation of cognitive functions of the studied participants [18]. This scale measures different domains of cognition and is a 30-point exam with a value of 25 or less is regarded as impaired cognitive functions [19]. Cases were grouped according to the MoCA score into two categories. The 1st group reported a cognitive disability test with a MoCA value

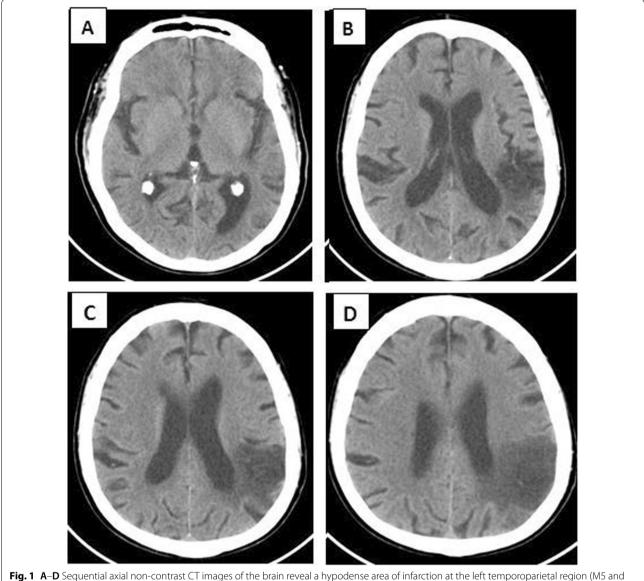


Fig. 1 A–D Sequential axial non-contrast CT images of the brain reveal a hypodense area of infarction at the left temporoparietal region (M5 and M6 regions); ASPECTS = 8

of 25 or less, and the 2nd group reported normal cognitive functions with a MoCA score over 25.

#### Statistical analysis

Data analysis was conducted using the Statistical Package of Social Science (SPSS) by IBM, Chicago, IL, USA, version 20, 2013 for Windows. Descriptive data were represented using numbers and percentages. Categorical variables were compared by the Chi-square test. Continuous variables have been shown as mean  $\pm$  SD for parametric data and median for non-parametric data.

Spearman correlation was carried out for correlation between ASPECTS, stroke severity (initial NIHSS) domains

of MoCA test, and biomarkers of cognitive impairment. Multivariate logistic regression analysis was carried out for the independent variables of cognitive impairment such as age, ASPECTS, initial INHSS, HTN and the biomarkers of cognitive decline such as ESR, CRP, S100B, MMP9, and glutamate were investigated. The collected data were analyzed using the SPSS Prism created.

### Results

# Clinical characters, initial NIHSS, and ASPECTS of ischemic stroke patients

One hundred and twenty patients were included in our research study, 63 males (52.5%) and 57 females (47.5%) with an average age of  $62.68 \pm 12.4$ . The frequent risk

**Table 1** Clinical characters, initial NIHSS, and ASPECTS ofischemic stroke patients

Variable	All patients
Number	120
Age (Y)	62.68±12.4
Male N (%)	63 (52.5%)
Hypertension N (%)	80 (66.7%)
DM N (%)	31 (25.8%)
Smoking N (%)	46 (38.3%)
Hyperlipidemia N (%)	18 (15%)
AF N (%)	20 (16.7%)
IHD N (%)	13 (10.8%)
Initial NIHSS (mean $\pm$ SD)	13.4±6.9
ASPECTS (Mean $\pm$ SD)	$7.11 \pm 2.43$

factors for ischemic stroke were hypertension (66.7%), smoking (38.3%), DM (25.8%), AF (16.7%), hyperlipidemia (15%), and ischemic heart disease (10.8%). The average initial stroke severity as determined by NIHSS was  $13.4\pm6.9$  and the mean ASPECTS value was  $7.11\pm2.43$  (Table 1).

#### Cognitive impairment in ischemic stroke patients

Of the ischemic stroke patients, 31 patients (25.8%) had diminished cognition, while 89 patients (74.2%) had preserved cognition. The average MoCA scores for cognitively disabled patients were considerably lower  $(21.72 \pm 2.93 \text{ vs } 26.02 \pm 3.21, P < 0.001)$  than for cognitively intact patients. The mainly affected sub-items of MoCA were lower executive functions (P = 0.005), lower attention (P=0.04), lower language (P=0.03), and lower memory (P=0.02). There were no significant differences between both groups of patients regarding educational level (P=0.9). Patients with diminished cognitive ability were older (P = 0.001) and had no substantial difference in sex (P = 0.76). Also, the average ASPECTS score in the cognitively disabled group of patients was significantly lower  $(5.46 \pm 3.84)$ vs  $8.32 \pm 1.33$  and P = 0.004) than for the cognitively intact group of patients (Table 2).

#### Stroke biomarkers of cognitive impairment

In cognitively affected patients, there has been a substantial rise in stroke biomarkers (including ESR, CRP, S100B, MMP9, and glutamate) relative to cognitively preserved patients (Table 2). Significant inverse relations have been observed regarding ASPECTS and cognitive impairment biomarkers (except for glutamate) (P < 0.05) (Table 3). Page 4 of 10

	Impaired	Preserved	P value
	cognition	cognition	
Number	31 (25.8%)	89 (74.2%)	
Age (Y)	$66.87 \pm 8.21$	$61.56 \pm 6.87$	P = 0.001
Gender (male)	17 (54.8%)	46 (51.7%)	P = 0.76
Education			
Illiterate	5 (16.1%)	14 (15.7%)	P = 0.9
Primary school	9 (29%)	22 (24.7%)	
Secondary school	6 (19.4%)	20 (22.5%)	
Tertiary school	5 (16.1%)	16 (18%)	
University educa- tion	6 (19.4%)	17 (19.1%)	
Biomarkers of cogn	itive impairment		
ESR	$32.9 \pm 28.5$	$18.7 \pm 16.8$	P<0.001
CRP	$7.1 \pm 2.29$	$3.94 \pm 1.1$	P<0.01
S100B	$136 \pm 39.24$	$95 \pm 29.2$	P<0.01
MMP 9 ng/ml	$417.5 \pm 122$	$212.6 \pm 79.8$	P<0.01
Glutamate nmol/l	$1.412 \pm 0.492$	$0.971 \pm 0.374$	P<0.01
MoCA test scores			
Visual–spatial ability	3.17±1.11	3.47±1.08	P=0.39
Naming	$2.32 \pm 0.57$	$2.42 \pm 0.77$	P = 0.51
Executive func- tions	$2.42 \pm 1.07$	$3.53 \pm 0.96$	P=0.005*
Attention	$4.34 \pm 1.23$	$5.69 \pm 1.34$	P=0.04 *
Language	$3.41 \pm 1.2$	$4.37 \pm 1.34$	P=0.03*
Memory	$3.08 \pm 1.27$	$3.75 \pm 1.43$	$P = 0.02^*$
Orientation	$5.69 \pm 0.3$	$6.09 \pm 0.38$	P = 0.12
Total MoCA score	$21.72 \pm 2.93$	$26.02 \pm 3.21$	P<0.001
ASPECTS	$5.46 \pm 3.84$	$8.32 \pm 1.33$	P = 0.004

# Table 2 Biomarkers of cognitive impairment and MoCA test scores in patients with cognitive impairment compared with patients with preserved cognition

# Correlation between MoCA, ASPECTS, and neurocognitive stroke biomarkers

In cognitively impaired patients, the aspects of language, attention, memory, and executive functions were significantly affected. But on the other hand, in cognitively disabled patients, the domains of visual–spatial ability, naming, and orientation were non-significantly reduced. Table 3 demonstrates significant inverse correlations linking mRS scores and MoCA test domains (executive functions, attention, memory, and language), as well as ASPECTS (P < 0.001 and P = 0.002, respectively). In addition, there was a significant inverse correlation linking values of MoCA test domains and most of the biomarkers of strokes (P < 0.05). Also, there were significant direct correlations linking ASPECTS and neurocognitive test domains (P < 0.05).

IS
nd MoCA domair
ker, ASPECTS, and
'e stroke biomaı
etween cognitiv
Correlation be
Table 3 Corre

	Executive functions	Memory	Language	Attention	ASPECTS	ESR	CRP	S100B	MMP9	Glutamate
Age										
r	- 0.44	- 0.37	- 0.35	- 0.33	-0.16	0.22	0.19	0.12	0.18	0.1
Ρ	< 0.05	< 0.05	< 0.05	< 0.05	0.24	0.15	0.21	0.28	0.26	0.31
Modified Rankin Scale	ıkin Scale									
r	- 0.81	- 0.82	— 0.80	- 0.75	- 0.73	0.63	0.53	0.49	0.55	0.45
Ρ	< 0.001	< 0.001	< 0.001	< 0.002	0.002	0.005	600.0	0.01	0.007	0.02
Executive functions	ictions									
r	ΝA	0.79	0.8	0.78	0.73	- 0.71	— 0.61	- 0.51	- 0.47	- 0.40
Ρ	ΝA	< 0.001	< 0.001	0.001	0.002	0.004	0.006	0.009	0.01	0.04
Memory										
	0.78	ΑN	0.75	0.72	0.62	- 0.61	- 0.60	- 0.55	- 0.51	- 0.41
Ρ	< 0.001	ΑN	< 0.001	0.003	0.006	0.006	0.005	0.007	0.009	0.04
Language										
,	0.80	0.75	ΑN	0.70	0.47	- 0.51	- 0.59	- 0.50	- 0.45	- 0.32
Ρ	< 0.001	< 0.001	ΑN	0.004	0.01	0.009	0.007	0.009	0.02	0.12
Attention										
r	0.78	0.72	0.70	ΝA	0.45	-0.47	- 0.60	— 0.49	- 0.49	- 0.30
Р	< 0.001	0.003	0.004	ΝA	0.02	0.01	0.005	0.01	0.01	0.13
ASPECTS										
	0.73	0.62	0.47	0.45	ΥZ	-0.75	- 0.51	— 0.40	- 0.39	- 0.29
Р	0.002	0.006	0.01	0.01	ΥN	< 0.001	0.009	0.04	0.04	0.14
ESR										
	- 0.71	- 0.61	— 0.51	— 0.47	-0.75	۲Þ	0.79	0.44	0.41	0.40
Ρ	0.004	0.006	0.00	0.01	< 0.001	ΥN	< 0.006	0.01	0.03	0.04
CRP										
	— 0.61	- 0.60	— 0.60	— 0.60	- 0.41	0.45	ΥN	0.42	0.45	0.41
Ρ	0.006	0.005	0.005	0.005	0.03	0.01	ΑN	0.03	0.01	0.04
S100B										
	- 0.51	-0.55	- 0.50	— 0.49	- 0.40	0.44	0.42	ΑN	0.41	0.39
٩	600.0	0.007	0.00	0.01	0.04	0.01	0.03	ΝA	0.03	0.04
MMP9										
	— 0.47	- 0.51	- 0.45	— 0.49	-0.39	0.41	0.45	0.43	ΑZ	0.35
Р	0.01	0.009	000	0.01	0.04	2003	0.01	000	N A	0 1 1

	S100B
	CRP
	ESR
	ASPECTS
	Attention
	Language
	Memory
(continued)	Executive functions
Table 3	

Glutamate

MMP9

∢ ∢ Z Z

0.35 0.11

0.39 0.04

0.04 0.04

0.40 0.04

— 0.29 0.14

- 0.30 0.13

-0.32 0.12

- 0.41 0.04

— 0.40 0.04

Glutamate r P

#### Outcome of ischemic stroke patients

According to mRS, our cases were divided into two groups: the first one includes 82 patients (68.4%) who had favorable outcomes (mRS 0–2), while 38 patients (31.6%) had poor outcomes. Patients with poor outcomes were older (P=0.001), more incidence of hypertension (P=0.001), and had no significant difference in sex (P=0.76). The average initial NIHSS for the favorable outcome group of patients was considerably lower than for the poor outcome group of patients (11.23±5.53 vs 17.81±7.65, and P<0.001). While the average ASPECTS score for the favorable outcome group of patients was higher than for the unfavorable outcome group of patients (8.12±1.76 vs 5.85±2.47, and P=0.001) (Table 4).

# Correlation of ASPECTS with MoCA, and outcome after 3 months of ischemic stroke

There was a strong positive correlation between the initial ASPECTS and total MoCA test score after 3 months follow-up from the onset of ischemic stroke (r=0.69 and P=0.003) as shown in Fig. 2a. Lower values of ASPECTS were accompanied by significantly poor outcomes compared to higher values of ASPECTS in the form of a significant negative correlation between the initial ASPECTS and modified Rankin Scale score after 3 months follow-up from the onset of ischemic stroke (r=0.39 and P=0.04) as shown in Fig. 2b.

## Correlation of the site of lesion with the cognitive decline (dominant or non-dominant hemisphere)

According to hemispheric dominance, patients with dominant hemisphere infarction showed significantly lower MoCA scores in comparison to patients with non-dominant hemispheric infarction ( $22.13 \pm 4.97$  vs  $24 \pm 3.84$ , P = 0.04), as shown in Fig. 3.

#### The independent variables of cognitive impairment

Lastly, the logistic regression analysis revealed that older age and ESR (OR 2.51, P < 0.001 and OR 2.33, P < 0.001, respectively) were the independent variables related with cognitive decline, followed by NIHSS (OR 2.23, P=0.001). ASPECTS and HTN also were linked with cognitive decline to a lesser extent (OR 2.12, P=0.005and OR 2.11, P=0.005, respectively). Other biomarkers of cognitive decline such as CRP, S100B, MMP9, and glutamate were less significantly associated with cognitive decline (P < 0.01) (Table 5).

#### Discussion

A rapid assessment of the clinical and radiological findings is needed for acute ischemic stroke (AIS). The ability to differentiate an acute CT infarction is beneficial in verifying the interpretation of acute stroke diagnosis [20].

#### Risk factors of acute ischemic stroke

In the current study, hypertension (66.7%), smoking (38.3%), DM (25.8%), AF (16.7%), hyperlipidemia (15%), and ischemic heart disease were common risk factors for stroke (10.8%). The analysis of Amelia et al. 2107 and Mahdi et al. 2018 is more or less identical to these results [21, 22]. In addition, multiple reports agree with our findings on standard risk factors like hypertension, diabetes mellitus, hyperlipidemia and smoking in about 80% of stroke patients [23–25].

# ASPECTS, stroke severity and the outcome of acute ischemic stroke

In our research, the ASPECTS score showed a negative relationship with the initial NIHSS that was close to the findings of David et al. 2005 reported a strong, linear, inverse relationship linking the initial NIHSS and ASPECTS; and each increase of ten points on initial NIHSS accompanied by a decrease of around 3 points on ASPECTS [26]. Additionally, Prabhakar and Kishore 2015 confirmed the ASPECT value's ability to anticipate the outcomes as measured by the NIHSS using CT scans through ASPECTS will also contribute to the prediction of the outcome of the stroke and the treatment of the stroke [27]. Subsequently, a better prognosis was correlated with patients with a score of more than seven in CT ASPECTS [28].

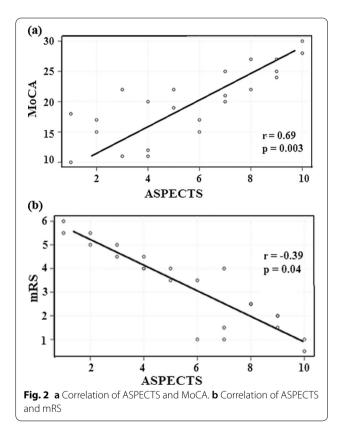
Our study revealed that substantial poor outcome results and higher mRS scores were correlated with older age, hypertension, high NIHSS, and decreased ASPECTS. In terms of favorable and unfavorable outcomes, sex, diabetes mellitus, dyslipidemia, IHD, and smoking did not differ significantly. Also, higher mRS, male, higher age, DM, smoking, HTN, AF, and depression were significant indicators of poor outcome in a large Swedish study of 15,959 stroke patients [29]. The much more significant factor affecting early and late outcomes is probably the severity of stroke on the clinical assessment. In general, in contrast to minor strokes accompanied by lesser initial NIHSS and higher ASPECTS, severe strokes with extreme initial NIHSS and lower ASPECTS have unfavorable outcomes [30].

#### Cognitive impairment in acute ischemic stroke

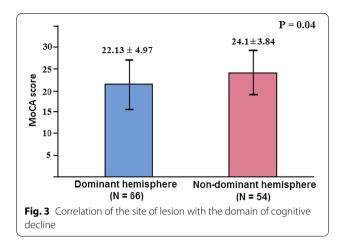
The incidence of cognitive impairment in our patients was 25.8%. In cognitively affected patients, there has been a substantial rise in stroke biomarkers (including

**Table 4**Correlation between stroke outcome according to mRSafter 3 months and risk factors, initial NIHSS, and ASPECTS

Variable	Favorable outcomes	Poor outcomes	P value
MRS	0–2	3–6	P value
Number	82 (68.4%)	38 (31.6%)	
Age (years)	$60.23 \pm 6.74$	$67.6 \pm 8.43$	P = 0.001
Male	41 (50%)	22 (57.8%)	P = 0.725
Hypertension	46 (56.1%)	34 (89.5%)	P = 0.001
DM	20 (24.4%)	11 (28.9%)	P = 0.511
Smoking	32 (39%)	14 (36.8%)	P = 0.729
Hyperlipidemia	11 (13.4%)	7 (18.4%)	P = 0.654
AF	13 (15.9%)	7 (18.4%)	P = 0.749
IHD	8 (9.7%)	5 (13.2%)	P = 0.778
Initial NIHSS	$11.23 \pm 5.53$	$17.81 \pm 7.65$	P<0.001
ASPECTS	8.12±1.76	5.85±2.47	P=0.001



ESR, CRP, S100B, MMP9, and glutamate) relative to cognitively preserved patients. Significant inverse relations have been observed regarding ASPECTS and cognitive impairment biomarkers (except for glutamate). The ASPECTS may be accompanied by serum and circulating blood biomarkers that indicate and clarify the pathophysiological reaction of the brain to the ischemic injury [31, 32]. The Zhong et al. [33]s study of 558 ischemic stroke



**Table 5** Multivariatelogisticregressionanalysisfortheindependent variables of cognitive impairment

Variables	O R	95% CI	Р
Age	2.51	1.91-3.24	P<0.001
HTN	2.11	1.37-2.67	P = 0.005
NIHSS	2.23	1.62-2.84	P = 0.001
ASPECTS	2.12	1.42-2.73	P = 0.005
ESR	2.33	1.76-3.11	P<0.001
CRP	1.89	1.42-2.43	P<0.01
S100B	1.77	1.14-2.22	P<0.01
MMP 9 ng/ml	1.65	1.03-2.12	P<0.01
Glutamate nmol/l	1.79	1.21-2.31	P<0.01

patients found that elevated matrix metalloproteinase-9 was associated with impairment of cortical functions. Increased MMP 9 promotes hematoencephalic barrier proteolysis and resulting in diffuse damage to the white matter of the brain [34]. Numerous researches have shown that there is a correlation regarding post-stroke cognitive impairment and C-reactive protein serum levels and ESR [35]. Excitotoxicity is a specific neuronal cell injury mechanism induced by hyperproduction of excitatory neurotransmitter [36]. Glutamate is a primary and exciting transmitter of many cognitive abilities, particularly the memory trail [37]. Leaks of neuron-specific components into liqueur and plasma are caused by acute ischemic brain damage [38]. Protein S100B is among the most researched neuro-specific biomarkers [39]. Christl et al. [40], indicated that CSF S100B could have a cognitive dysfunction diagnostic value, particularly at early phases of AD. Several logistic regression analyses revealed that the concentration of serum S100B was a statistically significant separate cognitive impairment marker [41].

#### **Correlation of ASPECTS and cognition**

A clear negative association regarding neurocognitive test scores (executive functions, attention, memory, and language) and stroke biomarkers (P < 0.05) was observed in our results. The identification of biomarkers in blood serum, plasma and cerebrospinal fluid (CSF) could also enhance the diagnostic and prognostic reliability of poststroke cognitive impairment [42]. Important negative associations between ASPECTS and cognitive disability biomarkers and positive significant relationships among ASPECTS and neurocognitive test domains were also found. One of the main complications following a stroke is post-stroke cognitive dysfunction, which is a subcategory of vascular cognitive impairment. Stroke has been expected to enhance cognitive impairment vulnerability by about five to eight times [43]. A large number of studies have already shown that in patients with stroke, cognitive performance can be used as a functional outcome predictor [44]. Hence, it is especially important for the diagnosis, treatment, and prognosis of post-stroke cognitive dysfunction, and has received a lot of attention among various researchers all over the world.

#### Correlation of the site of lesion with the cognitive decline

According to hemispheric dominance, patients with dominant hemisphere infarction showed significantly lower MoCA scores in comparison to patients with nondominant hemispheric infarction. These findings were similar to those of Chan et al. [45] who discovered that poor performance on the MoCA test by dominant cerebral hemisphere ischemic stroke patients likely reflects the MoCA test's reliance on both receptive and expressive language abilities, as well as verbal memory capacities.

#### Conclusions

ASPECTS is a convenient, easy-to-use and reliable scale to identify the extent of acute ischemic injury and can participate in assessing the outcome of acute ischemic stroke. Along with the findings of neuropsychological tests, ASPECTS and particular biomarkers of cognitive impairment will enable the early detection of post-stroke cognitive impairment. Therefore, the effective use of cognitive impairment treatment and preventive drugs would be suggested.

#### Abbreviations

AF: Atrial fibrillation; AIS: Acute ischemic stroke; ASPECTS: Alberta Stroke Program Early CT Score; CRP: C-reactive protein; CSF: Cerebrospinal fluid; CT: *Computed tomography*; DM: Diabetes mellitus; ESR: Erythrocyte sedimentation rate; GCS: Glasgow Coma Scale; HTN: Hypertension; ICH: Intracerebral hematoma; IHD: Ischemic heart disease; MCA: Middle cerebral artery; MMP9: Matrix metalloproteinase 9; MoCA: Montreal Cognitive Assessment; mRS: Modified Rankin Scale; NIHSS: *National Institutes of Health Stroke Scale*; SPSS: Statistical Package of Social Science.

#### Acknowledgements

None.

#### Authors' contributions

AE, ME, MA, and MF made substantial contributions to the study and participated in its design, acquisition, analysis, and interpretation of data. AA and NT participated in the analysis and interpretations of the radiological findings. SS participated in the analysis and interpretations of the study and the revisions of the manuscript. All authors read and approved the final manuscript.

#### Funding

This study received no funding.

#### Availability of data and materials

The datasets generated and analyzed during the current study are not publicly available due to institutional limitations, yet they are available from the corresponding author on reasonable request.

#### Declarations

#### Ethics approval and consent to participate

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration. Informed written consent was obtained from all individual participants included in the study. This study was approved by Mansoura Faculty of Medicine Institutional Research Board ("MFM-IRB"). Proposal Code: R.19.09.606—2019/09/04.

#### **Consent for publication**

Not applicable.

#### **Competing interests**

The authors declare that they have no competing interests.

#### Author details

<sup>1</sup>Neurology Department, Faculty of Medicine, Mansoura University, Mansoura 35516, Dakahlia, Egypt. <sup>2</sup>Radiology Department, Faculty of Medicine, Mansoura University, Mansoura, Egypt. <sup>3</sup>Neuropsychiatry Department, Faculty of Medicine, Port-said University, Port Fuad, Egypt.

Received: 16 June 2021 Accepted: 8 October 2021 Published online: 20 October 2021

#### References

- Piliszek A, Witkowski G, Sklinda K, Szary C, Ryglewicz D, Dorobek M, et al. Comprehensive imaging of stroke—looking for the gold standard. Neurol Neurochir Pol. 2016;50:241–50.
- Van Erp AC, Rebolledo RA, Hoeksma D, Jespersen NR, Ottens PJ, Nørregaard R, et al. Organ-specific responses during brain death: increased aerobic metabolism in the liver and anaerobic metabolism with decreased perfusion in the kidneys. Nat Sci Rep. 2018;8:4405.
- Hasan TF, Rabinstein AA, Middlebrooks EH, Haranhalli N, Silliman SL, Meschia JF, et al. Diagnosis and management of acute ischemic stroke. Mayo Clin Proc. 2018;93:523–38.
- 4. Powers WJ, Rabinstein AA, Ackerson T, Adeoye OM, Bambakidis NC, Becker K, American Heart Association Stroke Council, et al. Guidelines for the early management of patients with Acute Ischemic Stroke: a guideline for health-care professionals from the American Heart Association/American Stroke Association. Stroke. 2018;49:e46.
- Goyal M, Demchuk AM, Menon BK, Eesa M, Rempel JL, Thornton J, et al. Randomized assessment of rapid endovascular treatment of ischemic stroke. N Engl J Med. 2015;372:1019–30.
- Schröder J, Thomalla G. A critical review of alberta stroke program early CT score for evaluation of acute stroke imaging. Front Neurol. 2017;7:245.
- Esmael A, Elsherief M, Eltoukhy K. Predictive value of the alberta stroke program early CT score (ASPECTS) in the outcome of the acute ischemic stroke and its correlation with stroke subtypes, NIHSS, and cognitive impairment.

Stroke Res Treat. 2021, Article ID 5935170, 10 p. https://doi.org/10.1155/ 2021/5935170

- Gupta D, Sharma A, Uchino K, Alexandrov AV, Khan K, Shuaib A, et al. Accuracy of NIHSS in predicting the site of arterial occlusion in acute stroke: a Transcranial Doppler Study. J Stroke Cerebrovasc Dis. 2016;25:2109–15.
- Hill MD, Demchuk AM, Goyal M, Jovin TG, Foster LD, Tomsick TA, et al. Alberta Stroke Program early computed tomography score to select patients for endovascular treatment: Interventional Management of Stroke (IMS)-III Trial. Stroke. 2014;45:444–9.
- Sarraj A, Sangha N, Hussain MS, Wisco D, Vora N, Elijovich L, et al. Endovascular therapy for acute ischemic stroke with occlusion of the middle cerebral artery M2 segment. JAMA Neurol. 2016;73:1291–6.
- Esmael A, Elsherief M, Eltoukhy K. Prevalence of cognitive impairment in acute ischaemic stroke and use of Alberta Stroke Programme Early CT Score (ASPECTS) for early prediction of post-stroke cognitive impairment. Neurol Neurochir Pol. 2021;55(2):179–85. https://doi.org/10.5603/PJNNS.a2021. 0006.
- 12. Fanning JP, Wong AA, Fraser JF. The epidemiology of silent brain infarction: a systematic review of population-based cohorts. BMC Med. 2014;12:119. https://doi.org/10.1186/preaccept-3620022701268369.
- Hsieh YC, Seshadri S, Chung WT, Hsieh FI, Hsu YH, Lin HJ, et al. Association between genetic variants on chromosome 12p13 and stroke survival and recurrence: a one year prospective study in Taiwan. J Biomed Sci. 2012;3:19. https://doi.org/10.1186/1423-0127-19-1.
- Riverol M, Lopez O. Biomarkers in Alzheimer's disease. Front Neurol. 2011;2:46. https://doi.org/10.3389/fneur.2011.00046.
- Kuster GW, Dutra LA, Brasil IP, Pacheco EP, Arruda MJ, Volcov C, et al. Performance of four ischemic stroke prognostic scores in a Brazilian population. Arq Neuro-Psiquiatr. 2016;74:2.
- Pexman JH, Barber PA, Hill MD, Sevick RJ, Demchuk AM, Hudon ME, et al. Use of the Alberta Stroke Program Early CT Score (ASPECTS) for assessing CT scans in patients with acute stroke. Am J Neuroradiol. 2001;22:1534–42.
- Rowan MT, Wilson A, Dawson J, Quinn TJ. Functional assessment for acute stroke trials: properties, analysis, and application. Front Neurol. 2018;9:191.
- Nasreddine ZS, Phillips NA, Bédirian V, Charbonneau S, Whitehead V, Collin I, et al. The Montreal Cognitive Assessment (MoCA): a brief screening tool for mild cognitive impairment. J Am Geriatr Soci. 2005;53(4):695–9.
- Tan JP, Li N, Gao J, Wang LN, Zhao YM, Yu BC, et al. Optimal cutoff scores for dementia and mild cognitive impairment of the Montreal Cognitive Assessment among elderly and oldest-old Chinese population. J Alzheimers Dis. 2015;43(4):1403–12. https://doi.org/10.3233/JAD-141278.
- Etherton MR, Barreto AD, Schwamm LH, Wu O. Neuroimaging paradigms to identify patients for reperfusion therapy in stroke of unknown onset. Front Neurol. 2018;9:327.
- Boehme AK, Esenwa C, Elkind MS. Stroke risk factors, genetics, and prevention. Circ Res. 2017;120:472–95.
- Habibi-koolaee M, Shahmoradi L, Kalhori S, Ghannadan H, Younesi E. Prevalence of stroke risk factors and their distribution based on stroke subtypes in Gorgan: a retrospective hospital-based study—2015–2016. Neurol Res Int. 2018;4:1–7.
- 23. Kim JS. Unconventional, yet important, risk factors for stroke. J Stroke. 2018;20:1.
- 24. Bang OY, Ovbiagele B, Kim JS. Nontraditional risk factors for ischemic stroke: an update. Stroke. 2015;46:3571–8.
- Kim YD, Jung YH, Saposnik G. Traditional risk factors for stroke in East Asia. J Stroke. 2016;18:273–85.
- Kent DM, Hill MD, Ruthazer R, Coutts SB, Demchuk AM, Działowski I, et al. "Clinical-CT Mismatch" and the response to systemic thrombolytic therapy in acute ischemic stroke. Stroke. 2005;36:1695–9.
- 27. Abdelrasoul AA, Elsebaie NA, Gamaleldin OA, Khalifa MH, Razek AAKA. Imaging of brain infarctions: beyond the usual territories. J Comput Assist Tomogr. 2019;43:443–51.
- Khan M, Baird GL, Goddeau RP, Silver B, Henninger N. Alberta stroke program early CT score infarct location predicts outcome following M2 occlusion. Front Neurol. 2017;8:98.

- 29. Eriksson M, Norrving B, Terént A, Stegmayr B. Functional outcome 3 months after stroke predicts long-term survival. Cerebrovasc Dis. 2008;25:423–9.
- Ghosh K, Bhattacharya R, Ghosh S, Mahata M, Das S, Mondal G, et al. Predictors of severity and outcome and roles of intravenous thrombolysis and biomarkers in first ischemic stroke. Neuroimmunol Neuroinflamm. 2018;5:38–48.
- Mourão AM, Vicente LCC, Abreu MNS, Sant'anna RV, Meira DE, FCA, Xavier RMB, , et al. Clinical and molecular correlates of the ASPECTS in the acute phase of stroke. Arq Neuropsiquiatr. 2020;78(5):262–8. https://doi.org/10. 1590/0004-282x20200001.
- Sidorov E, Sanghera DK, Vanamala JKP. Biomarker for ischemic stroke using metabolome: a clinician perspective. J Stroke. 2019;21(1):31–41. https://doi. org/10.5853/jos.2018.03454.
- Zhong C, Bu X, Xu T, Guo L, Wang X, Zhang J, et al. Serum matrix metalloproteinase-9 and cognitive impairment after acute ischemic stroke. J Am Heart Assoc. 2018;7(1):e007776. https://doi.org/10.1161/jaha.117.007776.
- Wardlaw JM, Doubal F, Armitage P, Chappell F, Carpenter T, Muñoz Maniega S, et al. Lacunar stroke is associated with diffuse blood–brain barrier dysfunction. Ann Neurol. 2009;65:194–202. https://doi.org/10.1002/ana.21549.
- Mijajlović MD, Pavlović A, Brainin M, Heiss WD, Quinn TJ, Ihle-Hansen HB, et al. Post-stroke dementia—a comprehensive review. BMC Med. 2017;15(1):11. https://doi.org/10.1186/s12916-017-0779-7.
- Rueda CB, Llorente-Folch I, Traba J, Amigo I, Gonzalez-Sanchez P, Contreras L, et al. Glutamate excitotoxicity and Ca2+-regulation of respiration: role of the Ca2+ activated mitochondrial transporters (CaMCs). Biochim Biophys Acta. 2016;1857(8):1158–66. https://doi.org/10.1016/j.bbabio.2016.04.394.
- 37. Sonni S. Two generations with stroke and cognitive decline. Stroke. 2016;4:27–32. https://doi.org/10.1093/med/9780190497255.003.0005.
- Moulin S, Leys D, Schraen-Maschke S, Bombois S, Mendyk AM, Muhr-Tailleux A, et al. Aβ1-40 and Aβ1-42 plasmatic levels in stroke: influence of pre-existing cognitive status and stroke characteristics. Curr Alzheimer Res. 2015;14(6):686–94. https://doi.org/10.2174/1567205012666151027141730.
- Rezaei O, Pakdaman H, Gharehgozli K, Simani L, Vahedian-Azimi A, Asaadi S, et al. A new concept in neurocritical care. Iran J Neurol. 2017;16:83–9.
- Christl J, Verhülsdonk S, Pessanha F, Menge T, Seitz RJ, Kujovic M, et al. Association of cerebrospinal fluid S100B protein with core biomarkers and cognitive deficits in prodromal and mild alzheimer's disease. J Alzheimers Dis. 2019;72(4):1119–27. https://doi.org/10.3233/JAD-190550.
- Park BS, Lee HW, Lee YJ, Park S, Kim YW, Kim SE, et al. Serum S100B represents a biomarker for cognitive impairment in patients with end-stage renal disease. Clin Neurol Neurosurg. 2020;195:105902. https://doi.org/10.1016/j. clineuro.2020.105902.
- Zhang X, Bi X. Post-stroke cognitive impairment: a review focusing on molecular biomarkers. J Mol Neurosci. 2020;70(8):1244–54. https://doi.org/ 10.1007/s12031-020-01533-8.
- Kulesh A, Drobakha V, Kuklina E, Nekrasova I, Shestakov V. Cytokine response, tract-specific fractional anisotropy, and brain morphometry in post-stroke cognitive impairment. J Stroke Cerebrovasc Dis. 2018;27:1752–9. https://doi. org/10.1016/j.jstrokecerebrovasdis.2018.02.004.
- Almalki O, Alshehri MA, El-Sodany AM, El-Fiky AA. The awareness of healthcare staff towards post-stroke cognitive impairment: a cross sectional study. J Phys Ther Sci. 2018;30:883–7. https://doi.org/10.1589/jpts.30.883.
- Chan E, Altendorff S, Healy C, Werring DJ, Cipolotti L. The test accuracy of the Montreal Cognitive Assessment (MoCA) by stroke lateralisation. J Neurol Sci. 2017;15(373):100–4. https://doi.org/10.1016/j.jns.2016.12.028.

#### **Publisher's Note**

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.