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Evaluation of Recurrence of Ischemic Stroke and Transient Ischemic Attack Three Months After the First Transient Ischemic Attack Based On Diffusion-Weighted Imaging (DWI)

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ABSTRACT

Introduction:
One type of stroke is the Transient Ischemic Attack (TIA) which lasts less than twenty-four hours; of all patients, about 10 percent develop a stroke within three months after the first symptoms, and 30 percent develop over five years. Imaging is needed for differential diagnosis of this type of stroke. This study aimed to evaluate the recurrence of ischemic stroke and TIA three months after the first transient ischemic attack based on DWI results.

Materials and Methods:
This cross-sectional study was done on 135 TIA patients referred to Alavi Hospital in Ardabil City. All patients were examined at admission time by DWI imaging and laboratory tests and followed up three months later by phone and hospitalization, and necessary information was collected by a checklist.

Results:
The average $ABCD^2$ score in people with and without recurrence was 4.69 and 4.02, respectively. Also, the mean $ABCD^2$ score in individuals with abnormal DWI was significantly higher than in individuals with normal DWI (4.72 vs. 4.04, p=0.001). After the first TIA attack, patients with abnormal DWIs had a significantly higher recurrence of TIA and stroke in the first 90 days.

Conclusion:
This study showed that TIA patients with higher $ABCD^2$ scores in the first 24 hours based on DWI are more likely to have a recurrence of TIA or the onset of stroke within 90 days.

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Introduction

TIA is a transient stroke that lasts less than twenty-four hours and includes symptoms of motor, sensory, ataxia, diplopia, blurred vision, and speech disorders. Due to the transient symptoms, it is considered insignificant by patients and even some doctors (1). Many patients discontinue their treatment after a few months without consulting their doctor, who then goes to the hospital with symptoms of TIA or stroke, sometimes leading to disability or even death. Ten percent of patients develop a stroke within three months after the first symptoms and thirty percent over the next five years. Imaging is necessary for differential diagnosis. DWI may be positive in cases of TIA that last one hour and if it lasts more than six hours, the probability of becoming positive increases. Although the patient's clinical symptoms resolve in less than twenty-four hours, there may be changes in the imaging. The duration of symptoms, type of symptoms, risk factors, and imaging changes can play an important role in prognosis, and it is important to study the prognosis of these patients due to imaging changes. Awareness of risk factors is necessary to understand the cause of TIA and stroke because these factors effectively predict the risk of occurrence and develop preventive strategies (2). The risk of stroke immediately after TIA or minor stroke is significant. However, this is a challenge for clinical services because although most patients, by definition, suffer from a transient event without any immediate major problems, minorities are also at risk for stroke shortly after TIA. So, prognostic tools to identify high-risk patients have been developed for general education awareness, effective support for secondary care, and secondary preventive treatment (3).

Patients with stroke often report previous short-term neurological symptoms, and short-term data from population-based studies and trials show that approximately 20% of stroke patients have a previous TIA (4). In the past, the risk was considered low (approximately 1-2% per week and 2-4% per month) (5-7). Five risk factors were found to be independently associated with a higher risk of stroke recurrence at three months in a large group of TIA patients aged over 60 years (1 point), duration of symptoms between 10 to 60 minutes (1 point), and more than 60 minutes (2 points), clinical symptoms including motor weakness (2 points) and speech impairment (1 point), blood pressure above 140/90 (1 point) and diabetes mellitus (1 point) which were introduced as $ABCD^2$ score (8). $ABCD^2$ scoring system was obtained with 7 points and predicts stroke risk within seven days after TIA (9, 10).

DWI-MRI is a very sensitive method for detecting acute cerebral ischemia; therefore, it is possible that the presence of abnormalities in DWI in patients with TIA or minor stroke may suggest an active vascular process, such as a source of embolism or large arterial atherosclerotic disease and therefore show a greater risk of subsequent thromboembolism and consequent recurrent stroke (11). Approximately 50% of patients with TIA have focal abnormalities in DWI if scanned within the first 24 hours (12).

This study aimed to evaluate the recurrence rate of ischemic stroke and transient ischemic attack three months after the first transient ischemic attack based on DWI MRI imaging.

Materials and Methods

Study Design and Participants

This cross-sectional study was performed on all patients with transient stroke attack (TIA) referred to Alavi Hospital in Ardabil City from April 2020 to March 2021. This study examined patients with transient neurological symptoms (including motor symptoms, sensory, ataxia, diplopia, and speech disorders) by DWI and laboratory tests. Patients who were diagnosed with a transient ischemic attack and treated by a neurologist based on the mentioned clinical symptoms and imaging were selected and included in the study. Brain DWI was performed on patients, and patients who did not undergo DWI at the discretion of a neurologist were excluded from the study. The presence of a lesion in the brain based on DWI was considered in favor of positivity and the absence of the lesion was negative. Also, patients' information was collected by a checklist, including age, sex, $ABCD^2$ criteria, clinical symptoms, risk factors, imaging findings, and medications for treatment. Patients' information, including TIA recurrence, stroke recurrence, and clinical

symptoms, was followed up three months later by outpatient, hospitalization, or telephone and recorded in the relevant form. The diagnosis of TIA recurrence in this study was based on the recurrence of clinical symptoms of the disease, including the symptoms listed above (motor symptoms, sensory, and ataxia) in the three months after the first transient stroke.

Ethical Approval

This study was registered with the ethics committee of Ardabil University of Medical Sciences with the code IR.ARUMS. REC. 1399.071.

Statistical Analysis

Data were illustrated using descriptive statistical methods, including numbers, percentages, tables, graphs, and statistical indicators in SPSS version 21. Independent t-test was used to compare the average between the two groups (effect of $ABCD^2$ score on disease recurrence and effect of $ABCD^2$ score on DWI), and Chi-square and Fisher tests were used to examine the relationship between two qualitative data (relationship between DWI with TIA and stroke recurrence). A significant level in all tests was considered less than 0.05.

Results

In this study, 135 TIA patients were studied, 71 (52.6%) were male, and 64 (47.4%) were female. Of all patients, 106 (78.5%) had normal and 29 (21.5%) had abnormal DWI results. Out of 135 cases, 33 (24.4%) had recurrence after three months, and of the total recurrence cases, 13 were TIA (39.3%), and 20 (60.6%) were stroke. The average score of $ABCD^2$ score in individuals with general recurrence and abnormal DWI results was significantly higher than in other patients (Table 1). Also, out of the total cases, 8 (23.5%) had died, two of which were due to heart problems and six to stroke recurrence. Of the samples, 40 (29.6%) had blood pressure below 140/90. In terms of clinical symptoms, unilateral weakness with 93 cases (68.9%) was the most common symptom in patients. 27 patients (20%) had a history of diabetes, and in terms of duration of symptoms, 77 cases (57%) have been prolonged more than 60 minutes and 37 cases (27.4%) between 10 to 60 minutes and 21 cases (15.6%) less than ten minutes.

Table 1: The effect of ABCD2 score on overall disease recurrence

Variables		n	Average $ABCD^2$	Standard deviation	P-value
DWI results	normal	106	4.04	1.13	0.004
	abnormal	29	4.72	0.93	
Total recurrence of disease	Yes	33	4.69	1.01	0.003
	No	102	4.02	1.11	

Among those patients with abnormal DWI results, 21 (72.4%) patients, and among those patients with normal DWI, 12 (11.3%) had a total recurrence, and the relationship between DWI results and total disease recurrence was significant. Also, the relation between DWI results and TIA and Stroke recurrence was statistically significant (Table 2).

Table 2: The DWI results from disease recurrence

DWI results / Recurrence of disease		Normal		Abnormal		P-value
		n	%	n	%	
Total	+	12	11.3	21	72.4	0.001
	-	94	88.7	8	27.6	
TIA	+	5	4.7	8	27.6	0.001
	-	101	95.3	21	72.4	
Stroke	+	7	6.6	13	44.8	0.001
	-	99	93.4	16	55.2	

Of 135 CT scans, 18 (13.3%) were abnormal, and the rest were normal. Of those 18 cases, nine patients (50%) had a recurrence, and the rest did not. Also, 40 cases (29.6%) out of 135 patients had an abnormal cardiac echo, of which 40 cases had recurrence (30%). Out of the total sample, 38 patients (28.1%) had abnormal cervical Doppler ultrasound, of which 11 (28.9%) had a disease recurrence.

Discussion

In the present study, 135 patients referred to the hospital with their first TIA attack were studied, 71 (52.6%) male and 64 (47.4%) female. Of 135 patients, 106 (78.5%) had normal DWI, and 29 (21.5%) had abnormal DWI. In a similar study in 2004 by Purroy et al., out of 83 TIA patients who participated in the study and underwent DWI, 27 (32.53%) had DWI abnormalities (13).

In another retrospective study by Prabhakaran et al. (2007), 37 (25%) TIA patients had DWI abnormalities. This study showed that these abnormalities were independently associated with a higher risk of TIA or recurrent stroke in the hospital (14). $ABCD^2$ scoring is based on five risk factors that are independently associated with a higher risk of stroke recurrence in the first three months of TIA, including age over 60 years, duration of symptoms more than 10 minutes, dynamic weakness, speech impairment, blood pressure above 140/90 and diabetes mellitus (8).

The risk of recurrent stroke at three months varies from 0% in people who did not have any of these factors to 34% in people with all five risk factors. These factors are known to be associated with risk factors for early stroke.

This $ABCD^2$ score, with a total score of 7, is used to predict the risk of stroke during the seven days after TIA (9,10). In the present study, patients' $ABCD^2$ score was measured. It was shown that people with stroke and TIA recurrence in the first 90 days after the initial TIA had an average $ABCD^2$ score of 4.6. Those without recurrence had an average score of 4.0. On average, people with a higher $ABCD^2$ score had a higher recurrence rate, and people with a lower $ABCD^2$ score had a lower TIA or stroke recurrence. An $ABCD^2$ score could be a good predictor of the risk of recurrence of TIA or stroke within three months of the first TIA attack. In a similar study by Wardlaw et al., in 2015, 635 patients (63.5%) had a greater $ABCD^2$ score equal to 4 out of 1000 patients with TIA, of whom 52 patients (8.1%) had a recurrence of TIA in the first 90 days and 365 (36.5%) patients an $ABCD^2$ score less than 4, of which only 10 (2.7%) had a recurrence of TIA (15). Also, in another study conducted by Cutting et al. in 2016, 249 patients studied, 11 cases (4.4%) recurred during the first seven days, of which 8 were TIA, and 3 had a stroke. All 11 cases had a greater $ABCD^2$ score equal to 3, and none of the patients with an $ABCD^2$ score below three do not have neurological events (16). The present study showed that the average score of $ABCD^2$ was 4.7 in people with abnormal DWI, and in people with normal DWI, the average score was 0.4. Out of 34 patients with $ABCD^2$ scores less than 4, only two patients (5.9%) had abnormal DWI, and the remaining 32 (94.1%) had normal MRIs. However, out of 101 patients with an $ABCD^2$ score greater than or equal to 4, 27 (26.73%) had a lesion on their MRI. It may indicate that an $ABCD^2$ score below four may indicate a lower risk of recurrence of TIA or stroke within three months, and a larger score equal to 4 had higher risks, indicating the importance of the risk factors in the ABCD2 score in the decision to continue treatment of patients. The 2016 study by Cutting et al. also mentions that out of 249 patients, 211 underwent MRI, of which 61 (28.9%) had MRI-related lesions on their MRI. 30% of patients with $ABCD^2$ greater than 3 had a lesion on their MRI (16). Another study by Hozler et al. 2010 found that TIA patients with moderate to high $ABCD^2$ scores were more likely to have acute lesions on their DWI than those with low $ABCD^2$ scores (33.9% and 16.7%) (17).

In this study, it was also shown that out of 135 patients, 33 patients (24.4%) had recurrence during the first 90 days after admission, of which 13 cases (9.62%) with TIA and 20 cases (14. 81 %cases) has been a stroke, this may be due to patients not using the medication properly after discharge from the hospital and not seeing a doctor to renew the medication due to the coronavirus pandemic condition. In a 2000 study by Johnston SC et al., of all patients referred to

the emergency department with a diagnosis of TIA at a healthcare organization in California, USA, 1,707 patients, almost all of whom were in the hospital 24 hours after the accident, 428 patients (25.1%) developed vascular problems within 90 days of the TIA index, of which 44 (2.6%) complained of cardiovascular events, 45 patients (2.6%) died and 217 patients (12.6 %) have suffered from TIA (8). The present study showed that out of 33 patients who recurred within 90 days after TIA, 21 patients (63.6%) had abnormal DWI MRI, and twelve cases (36.4%) had normal DWI MRI. Of 102 patients without recurrence, 94 (92.2%) had normal MRIs, and 8 (7.8%) had abnormal MRIs. Out of 33 recurrences, 20 (60.7%) patients had stroke and 13 (39.3%) TIA recurrence, of which seven patients (35%) had normal MRI and 13 patients (65%) had abnormal MRI and in patients with recurrence of TIA, five patients (38.5%) normal MRI and eight patients (61.5%) abnormal MRI. Eight patients died during the study, of which 2 had heart problems and six suffered from stroke. Four (66.66%) of 6 patients had abnormal DWI MRI, and two (33.3%) had normal DWI. Also, the average score of $ABCD^2$ in these six patients was 5.16. It can be concluded that people who have an abnormal DWI are more likely to have a recurrent TIA or stroke than those who had a normal DWI at the beginning. From this and the data from other imaging mentioned in the previous studies, it can be concluded that DWI MRI is an appropriate imaging modality in patients with TIA symptoms.

In a 2005 study by Coutts et al., out of 120 TIA patients studied, 15 patients (12.5%) had a lesion on their MRI. Fourteen patients (11.7%) developed stroke in the first 90 days. Two patients died, one due to stroke and the other due to congestive heart failure, both of whom had lesions on their MRI. This study showed that a lesion on DWI is associated with a higher risk of new stroke during the first 90 days (18).

Limitations

The need for more accurate information from the patient may have affected the accuracy of the obtained information. We did not access some patients' contact information; therefore, we had to remove them from the study. Also, due to the recent pandemic conditions and the transient symptoms of TIA, many patients could not go to the hospital, which limited the data. The accuracy of DWI performed at Alavi Hospital can also affect the obtained data.

Conclusion

In summary, it can be concluded that TIA patients who have a higher $ABCD^2$ score or have a lesion in favor of TIA symptoms in the first 24 hours on DWI may have a higher rate of TIA recurrence or the onset of stroke within 90 days, after the first TIA attack. It can be used in triaging and treating TIA patients and medical advice to patients regarding risk factors.

Recommendations

Similar studies will be done on more patients for a longer time. Also, the association of lipid profile status and other tests of patients with recurrence of TIA or stroke can be assessed, and the patients' medical history should be considered in follow-up studies.

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