Zagazig University Medical Journals
www.zumj.journals.ekb.eg

Original Article

THE ROLE OF DIFFUSION-WEIGHTED AND FLUID ATTENUATED INVERSION RRECOVERY MAGNETIC RESONANCE IMAGING IN DIAGNOSIS AND TIMING OF ACUTE ISCHEMIC STROKE

May Selim Elgendy[1], Abdallah Almamun Sarhan[1]Elhady Ahmed Abd El Gawad[1], Alaa Ali Abdelghani[1], Ahmed Sabry Ragheb[2]

1Neurology Department, Faculty of Medicine, Zagazig University, Zagazig, Egypt
2 Diagnostic Radiology Department, Faculty of Medicine, Zagazig University, Zagazig, Egypt

Corresponding Author:
May Selim Safwat Elgendy
Neurology Department-Faculty of Medicine -Zagazig University,Zagazig, Egypt
maii.selim@yahoo.com

Submit Date	2019-02-22
Revise Date	2019-03-01
Accept Date	2019-03-07

ABSTRACT

Background: Ischemic stroke causes serious long-term disability and a great number of economic losses. Thrombolytic therapy is used only if the time of stroke onset was <4.5 hours. However, new categories such as wake-up and day un-witnessed strokes, patients unable to tell exact time of last seen well. The importance of study is to use diffusion weighted/Fluid attenuated inversion recovery (DWI/FLAIR) mismatch as a radiological marker which can help to identify patients with lacunar and non-lacunar stroke within 4.5 hours of onset and use it to determine whether patients with unknown onset stroke qualify for thrombolytic therapy or not.

Patients and methods: prospective cohort study was conducted on 72 patients with known time of symptoms onset, imaged within 24 hours from stroke onset. Patients underwent the admission Computed tomography CT and magnetic resonance scans (DWI and FLAIR only) with time gap was no longer than one hour. The presences of lesions in the neuroradiological modalities were assessed in correlation with the duration of the stroke.

Results: The time from stroke onset to neuroimaging was significantly shorter with ischemic lesions visible in DWI/FLAIR mismatch group when compared to other modalities. The DWI/FLAIR was characterized by global specificity 100%, sensitivity 91.9%, PPV 100% and NPV 92.1%. It succeeded to diagnose 12 patients with lacunar stroke before 4.5 hours from the stroke onset.

Conclusion: The presence of acute ischemic lesions only in DWI/FLAIR mismatch group can help to identify both lacunar and non-lacunar stroke patients who are within 4.5 hours' time window for intravenous thrombolysis**.**

Keywords: diffusion weighted/Fluid attenuated inversion recovery, Stroke

INTRODUCTION

Acute ischemic stroke (AIS) is highly prevalent disorder. Annually, >795,000 people in the United States experience AIS, 16% have a fatal outcome [1]. It causes a serious long -term disability, with 26% of ischemic stroke patients left dependent on caretakers for activities of daily living .It causes a great number of economic losses as the stroke related healthcare costs were estimated to exceed 38.6 billion dollars annually in the United States. From mortality, morbidity and economic stand-points; AIS prevention, early diagnosis and appropriate treatment are the keys to improve the outcomes [2]. Frequently, the exact time of stroke onset cannot be determined by reviewing the patient's history of last seen

well only especially in new categories such as wake-up and daytime-un-witnessed strokes which account 30% [3]. The goal of imaging evaluation is establishing the diagnosis as early as possible to obtain accurate information about the intracranial vasculature and brain perfusion for selecting the appropriate therapeutic interventions [4]. DWI provides potentially unique information on the viability of brain tissue. It provides image contrast which depends on the molecular motion of water which substantially altered by disease[5]. DWI is sensitive to shifts in water that occur between extracellular and intracellular compartments, this technique can demonstrate regions of brain that are undergoing ischemic injury during the first few minutes of focal neurological symptoms. In AIS, intracellular swelling occurs due to shifting the water from extracellular compartment causes initial increase in signal intensity. Other factors that contribute to increase in signal intensity are increasing tortuosity of extracellular and intracellular spaces and increase intracellular viscosity, these changes are caused by cytotoxic edema of the cell deprived of Adenosine Triphosphate [6]. Moreover, there is increasing evidence that the signal intensity of corresponding region in FLAIR images increases with time but may not be changed in the first 3-4 hours from the stroke's onset [7]. This leads to an interesting hypothesis that is called "DWI/FLAIR mismatch", i.e. the presence of abnormalities in DWI with a coinciding lack of relevant changes in FLAIR, may help to determine which patients' symptoms have persisted for <4 hours and making them suitable for reperfusion treatment[8]. DWI is superior in detecting very small ischemic lesions due to the high signal intensity-to-noise ratio [9]. DWI uses fast echo-planner imaging technology, it's highly resistant to patient motion and imaging time ranges from a few seconds to two minutes, so it's considered as a sensitive method for detection of transient ischemic events[10].

Aim of the work: is to evaluate DWI/FLAIR mismatch as a potential radiological marker which can help to identify patient with both lacunar and non-lacunar AIS within 4.5 hours of onset of neurological symptoms and determine whether patients with unknown time of onset are qualified for thrombolytic treatment or not.

Subject and methods: Cohort prospective study was conducted on 72 patients as comprehensive sample carried out at emergency room, MRI unit, stroke unit and intensive care unit of Neurology Department, Zagazig University Hospitals. Written informed consent was obtained from all participants and the study was approved by the research ethical committee of Faculty of Medicine, Zagazig University. The work was carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Inclusion criteria:

- All Patients with suspected AIS with focal neurological symptoms with known exact time between the onset of their neurological symptoms and the performance of neuroimagings and that time was <24 hours.
- CT and MRI on admission with time gap was <1 hour.
- National Institute of Health and Stroke scale (NIHSS) >3.

Exclusion criteria:

- Patients with head trauma.
- CT showing intracerebral hematoma or sub arachnoid hemorrhage.
- Lack of availability of MRI at admission.
- MRI contraindications such as pace-maker, titanium screw and intrauterine device.

All patients were subjected to:

1. Full history taking, stressing on exact time of neuroogical symptoms' onset, recording exact time between the onset of focal neurological symptoms and the performance of neuroimagings, an estimated time of stroke onset was clearly outlined in the patient data file and was based on interview with the patients if possible, their family members and the emergency team and door to needle time in patients were treated with thrombolytic therapy.

2. Detailed medical history stressing on risk factors of AIS.

3. Thorough general and Neurological examination.

4. Clinical and neurological scales encompassing:

- Glasgow Coma Scale (GCS): to assess level of consciousness
- NIHSS: to assess the severity of stroke.

Investigations:

A. Laboratory investigations*:* were done at Clinical Pathology Department, Zagazig university hospitals, including complete blood count, random blood sugar, electrocardiography,PT, PTT, INR, Kidney function test, liver function test, lipid profile and serum uric acid.

B. Radiological investigations: including CT and MRI (FLAIR& DWI Only) were performed consecutively upon the patient admission to emergency room with time gab <1 hour.

- **CT**: Using GE Pro Speed Dual Slice F II CT with MX135 Tube.
- **MR Imaging (We did only FLAIR and DWI films):** was done by using 1.5 Tesla super conducting MR imager (Achiva, Philibs Medical system). FLAIR was done first then DWI. Apparent diffusion coefficient (ADC) maps were automatically calculated by MRI machine software and included in the sequences.

First, we looked for lesions in DWI then we checked for presence of corresponding lesions in FLAIR.Lacunar strokes included and diagnosed by clinical and neuroradiological features(subcortical round DWI and FLAIR hyperintense lesions located deep in cerebral hemispheres or in the brain stem with total diameter <20 mm [11]. Dimension of non-lacunar infarcts were not measured in this study. FLAIR (positive) results were ruled for subtle hyperintense lesion corresponding to DWI lesion, if there were any interpretations between neurologist and a rater radiologist, a senior radiologist made the final decision.

We classified our patients into 3 groups based on the presence of acute ischemic parenchymal infarctions in the three radiological modalities:

- **Group (1):** Lesions were visible in DWI, FLAIR and CT.
- **Group (2):** Lesions were visible in both FLAIR and DWI only.
- **Group (3):** Lesions were visible only in DWI without corresponding changes neither in FLAIR nor in CT (DWI/FLAIR mismatch).

Secondly, we classified our patients according to the exact known onset of their focal neurological deficits into 3 groups:

- . **Group <4.5 hours of onset**: this group contained 37 patients.
- **Group >4.5<12 hours of onset**: this group contained 20 patients.
- **Group >12-24 hours of onset**: this group contained 15 patients.

Lastly, we classified our patients in study according to infarct size into:

- Lacunar strokes group.
- Non-lacunar stoke group.

All patients were treated according to our department protocol of acute ischemic stroke management:

- Thirty seven patients came before 4.5 hours and only ten patients were eligible to receive thrombolytic therapy according to its protocol of management.
- Sixty two patients were ineligible for rt.PA protocol of treatment so, we initiated stroke-blood pressure management protocol.

Statistical Analysis: Data were analyzed using IBM Statistical Package for Social Sciences (SPSS) advanced statistics, version 22 (SPSS Inc., Chicago, IL). Numerical data was described as mean and standard deviation. Comparisons between categorical variable performed using chi square test and fissure exact test when assumption of chi square not fulfilled. Independent sample t test was used to compare numerical variable between groups All tests were two sided. P-value < 0.05 was considered statistically significant(S), P-value<0.001 was considered highly statistically significant (HS), and p-value>0.05 was considered statistically insignificant (NS) [12].

Table 1 Descriptive demographic and clinical data of studied patients (N=72).

Variables		**N =72**	**%**
Groups	**Group 1**	6	8.3%
	Group 2	32	44.44%
	Group 3	34	47.22%
Sex	**Male**	33	45.8%
	Female	39	54.2%
Age			
Mean ± SD Range		62.14±12.02 (26.0-85.0)	
GCS			
Mean ± SD Range		13.18±2.07 (9.0-15.0)	
NIHSS			
Mean ± SD Range		15.14±5.78 (4.0-26.0)	
Receiving rt.PA	No	62	86.1%
	Yes	10	13.9%
Onset	<4.5 hour	37	51.4%
	>4.5-12 hour	20	27.8%
	>12-24 hour	15	20.8%
Onset / Hour		8.069±7.76 (1-24)	

Table 2 Detailed descriptive data, clinical data and classifications of studied patients among groups of radiological modalities (N=72).

Variables		**Group 1**		**Group 2**		**Group 3**	
		N=6	**%**	**N=32**	**%**	**N= 34**	**%**
Sex	Male	3	50.0%	11	34.4%	19	55.9%
	Female	3	50.0%	21	65.6%	15	44.1%
Age (Years)							
Mean ±SD Range		69.67±8.48 (55.0-79.0)		61.00±11.95 (26.0-25.0)		62.43±12.68 (40.0-85.0)	
GCS							
Mean ±SD Range		11.33±1.97 (9.0-15.0)		13.00±2.06 (9.0-15.0)		14.10±1.73 (9.0-15.0)	
NIHSS							
Mean ±SD Range		21.0±7.13 (7.0-26.0)		15.02±5.86 (4.0-25.0)		13.71±4.22 (5.0-24.0)	
Receiving rt. PA	No	6	100.0%	32	100.0%	24	70.6%
	Yes	0	0.0%	0	0.0%	10	29.41%
Time from onset	<4.5 hour	0	0.0%	3	9.37%	34	100.0%
	>4.5-12 hour	0	0.0%	20	62.5%	0	0.0%
	>12-24 hour	6	100.0%	9	28.12%	0	0.0%
Mean time from Onset /hours		22.50±1.64 (20.0-24.0)		11.36±6.79 (4.0-24.0)		2.15±1.0 (1.0-4.0)	
Infract size	Lacunar	0	0.0%	2	6.25 %	12	35.29%
	Non lacunar	6	100.0%	30	93.75%	22	64.7o%

Table 3 Risk factors of studied patients (N=72).

Risk Factors	No	%
Hypertension	47	65.27
Obesity	30	41.67
Diabetes mellitus	42	58.33
Old age	39	54.16
Pervious strokes	8	11.11
HCV positive patients treated with Sofosbuvir	26	36.11
Myocardial infarction	2	2.77
Atrial fibrillation	27	37.5
Ischemic Heart Disease	6	8.33
Rheumatic heart Disease	2	2.77
Smoking	40	55.55
Dyslipidemia	44	61.11

NB: more than one risk factor may be present in the same patient.

Table 4 Association between different radiological modalities groups and time of stroke onset (N=72).

Time of onset	**Group 1**		**Group 2**		**Group 3**		**X2**	**P value**
	N =6	**%**	**N=32**	**%**	**N=34**	**%**		
< 4.5 hour	0	0.0%	3	9.37 %	34	100.0%	80.23	<0.001 (HS)
> 4.5-12hour	0	0.0%	20	62.5%	0	0.0%		
> 12-24 hour	6	100.0%	9	28.12%	0	0.0%		

Table 5 The association between different radiological modalities and of size of infarction

Total No of cases (N=72)	**Group**						**X2**	**P value**
	Group 1		**Group 2**		**Group 3**			
	N =6	**%**	**N =32**	**%**	**N =34**	**%**		
Lacunar (N=14)	0	0.0%	2	6.25%	12	35.3%	9.25	0.005 (S)
Non lacunar (N=58)	6	100.0%	30	93.75%	22	64.7%		

Table 6 Association between age, GCS, NIHSS and onset of focal neurological symptoms and diagnosis of acute ischemic stroke among radiological modalities groups.
Factors sharing different letters are statistically different from each other

Variables	**Group 1**	**Group2**	**Group 3**	**F**	**P value**
	Mean ±SD	**Mean ±SD**	**Mean ±SD**		
Age	69.67±8.48	61.00±11.95	62.43±12.68	1.401	0.253 (NS)
GCS	11.33±1.97 a	13.00±2.06 ab	14.10±1.73 bb	5.14	0.008 (S)
NIHSS	21.0±7.13 a	15.02±5.86 b	13.71±4.22 b	4.059	0.022 (S)
Time of onset/ hour	22.50±1.64a (20.0-24.0)	11.36±6.79b (4.0-12.0)	2.15±1.0c (1.0-4.0)	62.745	<0.001 (HS)

Table 7 The evaluation of (group2) and (group 3) in diagnosing acute ischemic stroke within <4.5 hours of onset of their focal neurological symptoms and signs.

	Sensitivity	Specificity	PPV	NPV
Group 2	8.1%	77.1%	27.3%	44.3%
Group 3 (DWI/FLAIR mismatch)	91.9%	100.0%	100.0%	92.1%

DISCUSSION

Age is most important non-modifiable risk factor for AIS. Overall the risk of stroke is > doubles with each decade of increased age after 60 years of age at least up to age 84 **[13].** In this study we found that 39 out of 72 patients (54.16%) were older than 60 years and these results were similar to the results of **Abdel Ghani et al., 2011[13], Hirano et al., 2012[14].**

Regarding gender difference as a stroke risk, In our study we found that the stroke risk was slightly higher among females than males in patient and represents 54.2% % and 45.8% respectively and these were in agreement with **Somay et al, 2006[16]**.

In our study hypertension was the most important risk factor in AIS with the highest population-attributable risk at 65.27%.This was in agreement with **Yang et al., 2014[17]**.

In this study dyslipidemia was the second most common risk factor among our patients as we found 44 patients (61%) were dyslipidemic and these results were in accordance with **Grace et al., 2016[18]**. On the other hand most of epidemiological studies failed to find a direct association between total cholesterol and stroke risk **Giang et al., 2013[19].**

In our study we observed that 26 out of 72 patients (36.11%) gave history of they were still under treatment with Sofosbuvir or just finished this treatment one month before acute focal neurological symptoms. This finding raises the question of whether hepatitis C virus (HCV) infection itself or the treatment with the Sofosbuvir was responsible for this high percentage,considering that the HCV prevalence reached 13% among the Egyptian population **Kamal and Abdelhakim 2018[20].**

In our current study we assumed that the mean time between the acute focal neurological symptoms' onset and the neuroimaging was highly significantly shorter in patients from group 3 when compared to the mean time for patients from group 2 and group 1. In group 3 (the presence of acute ischemic lesions which presented only in the DWI and there were no relevant changes in the crossponding FLAIR and CT), i.e. "DWI/FLAIR mismatch" the mean time (±SD) of 2.15(±1.0) from symptoms' onset and neuroimaging and ranged between 1-4 hours. However, in patients from group 2 (the presence of acute FLAIR hyperintensities crossponding with the changes found in DWI) the mean time (±SD) of 11.36(±6.79) from the neurological symptoms' onset and the neuroimaging and ranged between 4.0-24.0 hours. In group 1 (the present of lesions in CT in crossponding to lesions in found in the DWI and in the FLAIR) the mean time (±SD) of 22.50(±1.64) from the neurological symptoms' onset and neuroimaging and ranged between 20-24 hours and it was the longest among neuroimaging modalities groups. These results were in agreement with the results of **Thomalla et al., 2011[7] and Grezegorz et al., 2014[21]**.

Alejandro et al., 2013[15] evaluated the accuracy of DWI in the diagnosis of AIS and reported that DWI demonstrated a sensitivity of 90% and specificity of 97% in detection of AIS and exclusion of patients with stroke mimics. The current study evaluated the accuracy of DWI/FLAIR mismatch in the diagnosis of AIS within 4.5 hours. The DWI/FLAIR mismatch group was very effective in diagnosis of 34 patients out of 37 patients came and imaged <4.5 hour of onset of their focal neurological symptoms with specificity 100%, sensitivity 91.9%, PPV 100% and NPV 92.1%. The slight decrease in sensitivity was due to the presence of early FLAIR hyperintensities crossponding to lesions in DWI in 3 patients out of 37 who were imaged <4.5 hours from stroke onset. Previous studies reported a specificity and

sensitivity of DWI/FLAIR mismatch of 97 % and 94 % **(Petkova et al., 2010)** [22], 78% and 62 % **(Thomalla et al., 2011)** [7], 98% and 58% **(Grezegorz et al., 2014)** [21] respectively. These variations among results may be due to different sample size, type of study and using different MRI protocols. Among this group only 10 patients treated by thrombolytic therapy while the remaining patients were illegible regarding the guidelines protocol of thrombolytic therapy.

Regarding the 32 patients of group 2(FLAIR shows hyper-intestines in corresponding to lesions in DWI without relevant changes in CT), 9 out of these 32 patients (28.12%) were imaged within 12-24 hours, 20 patients (62.5 %) were imaged within >4.5- 12 hours and there were 3 patients (9.37%) were imaged before 4.5 hours. This may be caused mainly by the pathomechanism of hyperintense signal in T2- image sequences. The net increase in tissue water, an element of vasogenic edema, become detectable in FLAIR and T2 sequences 3 hours after onset of ischemic events[23].This slight decrease in sensitivity of DWI/FLAIR mismatch may suggest that if this modality was to be considered as a "tissue clock", only patients with a positive DWI result and negative FLAIR result should be considered viable for thrombolytic therapy, this however, may result in disregarding a group of patients who may also remain within the time window for thrombolytic treatment, but in whom some acute lesions are found in FLAIR[21].

In fact, DWI/FLAIR mismatch's performance has shown dependence on the variability in magnetic susceptibility effect which is based on different magnet field strength or MRI sequence parameters, which can significantly diminish the sensitivity of DWI/FLAIR mismatch when FLAIR images are acquired on 3.0 Tesla scanners. Despite these variabilites, DWI/FLAIR mismatch's ability to narrow stroke onset to the first 3 to 4.5 hours which allows a subset of stroke of unknown onset such as wake up stroke or day un witnessed stroke to be considered for thrombolysis[24].Most researches have attempted to address this problem by assuming that subtle FLAIR hyper intestines corresponding to acute DWI changes should not disqualify from thrombolytic treatment and they suggested many methods to improve the accuracy of FLAIR hyper intensity assessments e.g. calculation of relative signal intensity[25] combined with advanced quantitative image analysis applied to FLAIR[22] or T2-weighted images, but all of these methods applied only for research purpose as they were too complicated if applied in an emergency settings[26].

In our study DWI/FLAIR mismatch succeeded to identify small and deep ischemic lesions which cause lacunar syndromes as lacunar strokes were diagnosed in 14 patients out of 72 patients of acute ischemic lesions with a percentage of 19.4%, 12 patients out of 14 patients were imaged <4.5 hours and diagnosed via group 3(DWI/FLAIR mismatch) and only 2 cases diagnosed within >4.5 <12 hours within group 2(FLAIR shows lesions in corresponding to DWI) and this were nearly similar to **Grezegorz et al., 2014**[21]. In most studies regarding the role of DWI/FLAIR mismatch; lacunar strokes were to some extent but not always represented [27][25][22].

CT brain positive results corresponding to DWI and FLAIR lesions (group 1) were found in 6 out of 72 patients imaged within 20 -24 hours and all were non-lacunar lesions. The visibility of lesions in CT depended significantly on the time of the stroke onset with mean time (±SD) of 22.50(±1.64), infarct size, severity of stroke with a mean admission NIHSS (±SD) of 21.0(±7.13) and decreased conscious level with GCS mean (±SD) of 11.33(±1.97) in comparison to group 2 and group 3. Our result regarding this group were in disagreement with results of **Grezegorz et al., 2014**[21], who reported that CT has detected lacunar lesions. On the other hand, our current study agreed with them in considering CT as the first line imaging modality in emergency room. However, its result was frustrating because it was less useful as a lesion identification tool and instead it was used to exclude intracerebral hemorrhage and sub-arachnoid hemorrhage.

The main limitation of our study was the relatively small sample size, which prevented the acquisition of more reliable statistical estimation regarding lacunar strokes. The FLAIR analysis against DWI may have an impact on the assessment of acute ischemic

changes; it has been suggested that for increased reliability, researches examining FLAIR images should be blinded to results of DWI [28] [29]. However, our study procedure reflected the way of thinking in emergency settings, where it was more efficient to us to analyze FLAIR after DWI scans, also because FLAIR frequently reveals prior vascular abnormalities.

CONCLUSION

The result of our study support the utility and efficacy of DWI/FLAIR mismatch in detection the onset time of strokes in hyper acute phase not only limited to large territorial infarcts, but also including lacunar syndromes

Declaration of interest
The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.
Funding information
None declared

REFERENCES

1. **Jauch EC, Saver JL, Adams JR et al**: Guidelines for the early management of patients with acute ischemic stroke: a guideline for healthcare professionals from American Heart Association/ American Stroke Association. Stroke 2013; 44:870-947.
2. **Stem GM, Van Hise N, Urben LM et al:** Thrombolytic therapy in wake up stroke patients. Clin Neuropharmacol 2017; 40(3): 140-146.
3. **Deborath L, Pedro R, Pedro F et al:** Wake-up stroke: Clinical characteristics, sedentary lifestyle, and daytime sleepiness. Rev. Assoc. Med. Bras 2016; 62 (7): 628-634.
4. **Srinivasan A., Goyal M, Al Azri F et al:** State of art imaging of acute stroke.Radiographic *2006;* 26:75-96.
5. **Manabu I, Jean M O., Julien L. et al:** Impact of Diffusion-Weighted Imaging Alberta stroke Program Earl computed Tomography Score on the success of endovascular reperfusion therapy. Stroke 2014; 45:1992-1998.
6. **Emeriau S, Serre I, Toubas O et al:** Can diffusion-weighted imaging-fluid attenuated inversion recovery mismatch (positive diffusion-weighted imaging/negative fluid-attenuated inversion recovery) at 3 Tesla identify patients with stroke at 4, 5 hours? Stroke 2013; 44: 1647-1651.
7. **Thomalla G,Cheng B,Ebinger M et al :**DWI/FLAIR mismatch for the identification of patients with acute ischemic stroke within 4.5 h of symptoms onset (PRE-FLAIR): a multicenter observional study. Lancet Neurol 2011; 10(11):978-986.
8. **Kim BJ, Kim JH, Lee DH et al:** Diffusion- weighted image and fluid-attenuated inversion recovery image mismatch: unclear-onset versus clear-onset stroke. Stroke2014; 45: 450-455.
9. **Wintermark M,Albers G, Broderick JP et al :** Acute stroke imaging research roadmap II. Stroke 2013; 44(9):2628-2639.
10. **Sylaja P , Coutts S , Krol A et al :** Vision study group; when to expect negative Diffusion-Weighted images in stroke and transient ischemic attack. Stroke 2008; 39: 1898-1900.
11. **Potter G, Fregal J and Joanna M:** Wide variation in definition, detection and description of lacunar lesions on imaging. Stroke 2011; 42:359-366.
12. **Gorden M:** Determining the number of factors to retain in EFA: Using the SPSS R-Menu v2.0 to make more judicious estimations. Practical assessment, research and evaluation 2013; 18(8):60-74.
13. **Abdel Ghani A, Zaitoun A and Gawish H:** Prognostic Value of D-Dimer in Diffusion Weighted-MRI Defined Early Ischemic Stroke Recurrence. Egypt Journal of Neurology, Psychiatry and Neurosurgery 2011; 48: 215-222.
14. **Hirano K, Takashima S, Dougu N et al:** Study of hemostatic biomarkers in acute ischemic stroke by clinical subtype. Journal of Stroke and Cerebrovascular Diseases 2012; 21(5): 404-410.
15. **Alejandro M, Arnold H, Sergio I et al:** Accuracy of diffusion weighted imaging in the diagnosis of stroke in patients with suspected cerebral infarcts. Stroke 2013; 44(4):1169-1171.
16. **Somay G, Topaloğlu P, Somay H et al:** Cerebrovascular risk factors and stroke subtypes in different age groups: a

hospital-based study. Turk J Med Sci 2006; 36(1): 23-39.

17. **Yang X, Gao S, Ding J et al:** Plasma D-dimer predicts short-term poor outcome after acute ischemic stroke. PLOS ONE 2014 ;(2):1-7.
18. **Grace M, Jacob K, Kumar A et al:** Role of dyslipidemia in ischemic and hemorrhagic stroke, a case control study International Journal of Advances in Medicine 2016; 3(3); 694- 698.
19. **Giang K, Bjorck L, Novak M et al:** Stroke and coronary heart disease: predictive power of standard risk factors into old age—long-term cumulative risk study among men in Gothenburg, Sweden. European Heart Journal 2013; 34(14): 1068–1074.
20. **Kamal S and Abdel Hakim S**: Hepatitis C in developing countries, current and future challenges. Hepatitis C in Egypt, 1st edition, Elseiver inc; pp: 41-5.
21. **Grzegorz W, Piliszek A, Skierczyńska A et al:** The usefulness of diffusion-weighted/fluid-attenuated inversion recovery imaging in the diagnostics and timing of lacunar and non-lacunar stroke. Neuroradiologyv2014; 56(10):825-831.
22. **Petkova M, Rodrigo S, Lamy C et al:** MR imaging helps predict time from symptoms onset in patients with acute stroke: Implications for patients with unknown onset time. Radiology 2010; 257:782-792.
23. **Perkins C, Kahaya E, Rouge C et al:** Fluid attenuated inversion recovery and diffusion- perfusion weighted abnormalities in 117 consecutive patients with stroke symptoms. Stroke 2001; 32:2774-2781.
24. **Jenny P and Gregory W;** Wakeup stroke: Current understanding. Top Magan REson Imaging 2017; 36(3):97-102.
25. **Ebinger M, Galinovic I, Rozanski M et al:** Fluid attenuated inversion recovery evulsion within 12 hours from stroke onset: a reliable tissue clock? Stroke 2010; 41:250-255.
26. **Siemonsen S, Mouridsen K, Holst b et al:** Quantitative T2 values predict time from symptom onset in acute stroke patients. Stroke 2009; 40:1612-1616.
27. **Thomalla G, Rossbach P, Rosenkranz M et al:** Negative fluid-attenuated inversion recovery images identify acute ischemic stroke at 3 hour or less. Ann Neurol 2009; 65(6):724-732.
28. **Aoki J,Kimura K, Iguchi Y, Shibazaki K, Saki K, et al:** FLAIR can estimate the onset time in acute ischemic stroke patients. J Neurol Sci 2010; 293(1-2):39-44.
29. **Koichiro N, Aoki J, Sakamoto Y and Kimura:** About 30% of wake-up stroke patients may be candidate for the rt.PA therapy using Negative-FLAIR as a "tissue clock". Journal of the Neurological Sciences 2017;15 (382):101-104.

To cite this article: Elgendy MS, Sarhan AA, Abd El Gawad EA, Abdelghani AA, Ragheb AS.The role of diffusion-weighted and fluid attenuated inversion rrecovery magnetic resonance imaging in diagnosis and timing of acute ischemic stroke.,Egypt.ZUMJ 2019;25(3);447-455,DOI: 10.21608/zumj.2019.7674.1065