The Value of Diffusion-Weighted MRI in CT-Negative Stroke Mimickers

İnmeyi Taklit Eden BT Negatif Klinik Durumlarda Diffüzyon Ağırlıklı MRG'nin Değeri

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ABSTRACT Objective: The purpose of the study is to assess the diagnostic accuracy of diffusion- weighted magnetic resonance imaging (MR-DWI) performed in the first six hours after symptom onset in patients mimicking stroke. **Material and Methods:** The patients included in the study were those in whom the non-contrast computed tomography (NCCT) scan failed to depict the reason for the new stroke-like symptoms and/or the patients for whom additional information was needed in order to plan their therapy. Patients who had an imaging technique performed within six hours after presenting in the ED were included. Final diagnosis of stroke was derived from any of the positive results of MRI, NCCT, data derived from patient's files or telephone follow up, asking whether the patient experienced a stroke attack within three months after index ED visit. **Results:** Data of 78 patients were analyzed and ischemic stroke was detected in 17 patients. The sensitivity and specificity of MR-DWI were 100% (95% CI: 80-100) and 100% (95% CI: 94-100), respectively. The positive and negative predictive values for MR-DWI were 100 (95% CI: 80-100) and 100 (95% CI: 94-100), respectively. **Conclusion:** MR-DWI is a fast and valuable imaging modality in the ED. The results of the test can be used in daily practice of busy EDs. The test can change the management strategy of NCCT negative patients with new stroke-like symptoms when a decision about patient treatment requires additional information.

Key Words: Stroke; diffusion magnetic resonance imaging

ÖZET Amaç: Çalışmanın amacı inmeyi taklit eden klinik durumlarda semptomların başlamasından sonraki 6 saatlik süreçte yapılan diffüzyon ağırlıklı Manyetik Rezonans Görüntüleme (MR-DWI)'nin tanıdaki doğruluğunu karşılaştırmaktır. **Gereç ve Yöntemler:** Çalışmaya dahil edilen hastalar kontrastsız Bilgisayarlı Tomografi (NCCT) taramasının inmeyi taklit eden ve yeni başlangıçlı semptomların nedenini bulamadığı ve/veya tedaviye karar vermek için ek bilgi gereken hastalardı. Acil ünitesine başvurduktan sonraki 6 saat içinde görüntüleme yapılan hastalar çalışmaya alındı. Nihai inme tanısı pozitif MRI, NCCT, hasta dosyalarındaki veriler veya telefon takibi yoluyla ilk vizitten sonraki üç ay içinde hastanın inme atağı geçirip geçirmediğini sormak suretiyle elde edildi. **Bulgular:** 78 hastaya ait veriler analiz edildi ve iskemik inme 17 hastada tespit edildi. MR-DWI duyarlılık ve özgüllüğü sırasıyla %100 (95 GA: %80-100) ve %100 (%95 GA: 94-100) idi. MR-DWI için pozitif ve negatif prediktif değerler sırasıyla 100 (%95 GA: 80-100) ve 100 (%95 GA: 94-100) idi. **Sonuç:** MR-DWI acil ünitesinde hızlı ve değerli bir görüntüleme yöntemidir. Test sonuçları yoğun acil servislerde günlük uygulamada kullanılabilir. Test yeni başlangıçlı ve inmeyi taklit eden semptomları olan NCCT negatif hastaların tedavisine karar vermek için ek bilgiye ihtiyaç duyulduğunda tedavi stratejisini değiştirebilir.

Anahtar Kelimeler: İnme, felç; difüzyon manyetik rezonans görüntüleme

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Stroke survival is associated with significant medical, social, and economic burden. Approximately 15% of patients suffering a stroke require hospitalization for their further nursing care, and more than 40% are disabled.[1]

Immediate recognition of symptoms by patients and treatment of stroke by emergency physicians or a stroke team are critical for improving stroke outcomes and reduction of risk morbidity and mortality.[1]

The timely diagnosis of acute cerebral ischemia has become critical with the advent of reperfusion therapy. Intravenous fibrinolytic therapy is indicated in the first three hours after symptom onset.[2] Patients presenting to emergency departments (ED) with the symptoms compatible with stroke must be assessed for eligibility of reperfusion therapy in a limited time window.[3] National Institutes of Health (NIH) score must be calculated and neuroimaging must be performed and interpreted as soon as possible to reduce the thrombolytic delivery time. In case of thrombolytic therapy, misdiagnosis of the patient has potentially important clinical and medicolegal implications such as increased risk of intracranial hemorrhage and malpractice claims.

Noncontrast computed tomography (NCCT) is the first imaging modality in acute stroke in the ED. NCCT is able to differentiate hemorrhagic stroke from ischemic stroke and can also exclude other potential causes of acute neurological symptoms.

An early pathologic process in stroke, shift of water from the extracellular space into the intracellular space because of adenosin triphosphate loss, can be sensitively detected by diffusion-weighted MR (MR-DWI).[4] There are studies showing that MR-DWI may offer high sensitivity early in the course of stroke.[4]

The purpose of this study is to assess the diagnostic accuracy of MR-DWI performed in the first six hours after symptom onset in patients mimicking stroke.

MATERIAL AND METHODS

This is a retrospective cohort study in patients with stroke-like symptoms in an ED setting. We reviewed all the MR-DWIs obtained between January 2007 and December 2008 in the ED of a University Hospital with an annual census of approximately 70 000 adult patients. The routine procedure in the ED is to order NCCT for the patients with signs and symptoms compatible with stroke, and regardless of the result of NCCT, to hospitalize the patient. The patients included in the study were those in whom the NCCT scan failed to depict the reason for the new stroke-like symptoms and/or the patients for whom additional information was needed in order to plan their therapy. According to the consultation policy of our hospital, all patients were consulted by a senior Neurology resident under the supervision of a faculty member after NCCT, but before MR-DWI. The need for a MR-DWI was decided together. Patients who had an imaging technique performed within six hours after presenting to the ED were included. Patients were excluded if a basic MRI scan had been ordered. All CT and MR-DWIs were interpreted by a radiology resident under the supervision of a faculty member. NCCT scans and MR-DWIs were interpreted by two seperate teams. Final diagnosis of stroke was derived from any of the positive results of MRI, CT, data derived from patient's files or telephone follow up, asking whether the patient experienced a stroke attack within three months after index ED visit.

MRI was performed with a 1.5 T unit (Philips Intera, Eindhoven, The Netherlands) with echoplanar capabilities. NCCT was performed with spiral or multislice scanners (Toshiba XVision and Toshiba Aquillon 64). We obtained 5-mm-thick contiguous sections. All CT images were also interpreted by a radiology resident and faculty member of Radiology.

STATISTICAL ANALYSIS

The study data were analyzed using SPSS 15.00 for Windows (SPSS Inc., Chicago, Illinois, USA) and MedCalc 11.2 (MedCalc Software, Mariakerke, Belgium). Demographic characteristics were summarized as a mean ± SD for continuous variables and as a percentage of the group for categorical variables. Nonparametric comparison of the two groups

was performed by Mann-Whitney U test and $\chi 2$ test for categorical variables. The normality analysis was performed by Kolmogorov-Smirnov test. Sensitivity, specificity, and positive and negative predictive values and their 95% confidence intervals were calculated for MR-DWI.

RESULTS

Between January 2007 and December 2008 , a total of 108 MR-DWI were ordered. Thirty of 108 patients were excluded either for CT imaging was not performed or for patients were presented to the ED more than six hours after symptoms onset (Figure 1). The mean age of the study population was 56 ± 18 years and 56% of the patients were males. MR-DWI detected acute stroke in 17 out of 78 patients (Table 1). Demographic and baseline characteristics of the patients are listed in Table 2. There were two patients with false positive NCCT results. The reports of these two cases were interpreted as cortical sulcal effacement.

The sensitivity and specificity of MR-DWI were 100% (95% CI: 80-100) and 100% (95% CI: 94-100), respectively. The positive and negative predictive values for MR-DWI were calculated as 100 (95% CI: 80-100) and 100 (95% CI: 94-100), respectively.

DISCUSSION

In the study of Kothari et al., misdiagnosis rate of stroke by emergency physicians have ranged from 5% to 33%.[5] In the study of Ferro et al., misdiagnosis rate was reported as 9%.[6] In an other study, 19% of 441 patients who were initially diagnosed as stroke by a stroke team had a condition mimicking stroke. Emergency physicians have a responsibility to distinguish stroke patients from stroke mimickers, and as a member of stroke team, should begin thrombolytic therapy to eligible patients in a limited time window. Clinical assessment is insufficient to differentiate ischemic from hemorrhagic stroke or to identify all contraindications for therapy.[7]

In a meta-analysis, the sensitivity, specificity, and positive and negative predictive values of MR-DWI and NCCT were compared. For MRI with

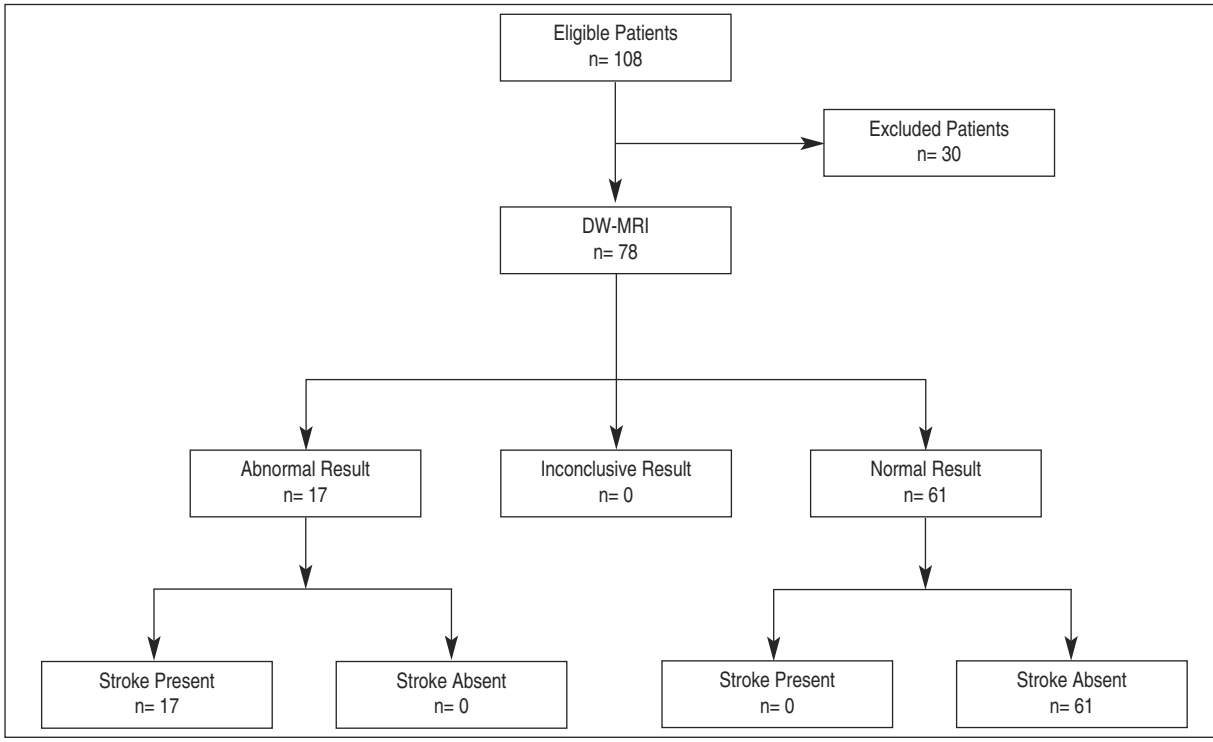

FIGURE 1: Flow diagram of the patients.

TABLE 1: Test results of NCCT and MR-DWI.

		NCCT			MR-DWI	
		Normal	Abnormal	Inconclusive	Normal	Abnormal
Stroke	Negative	59	0	2	61	0
	Positive	17	0	0	0	17

DWI, the sensitivity was 97% (95% CI: 94-98), specificity was 100% (95% CI: 88-100), positive predictive value (PPV) was 100% (95% CI: 98-100), and negative predictive value (NPV) was 91% (95% CI: 75-98). The sensitivity of NCCT was 47% (95% CI: 43-51), specificity was 93% (95% CI: 85-97), PPV was 97% (95% CI: 94-99) and NPV was 23% (95% CI: 19-28) (Table 3).[7]

A prospective study compared MR-DWI with NCCT in the ED patients with suspected stroke and found that MR-DWI detected acute stroke (both ischemic and hemorrhagic) and chronic hemorrhage more frequently than CT.[8] In this study, acute ischemic stroke was detected in 46% of the patients with MR-DWI and 10% of the patients with NCCT. Using the clinical diagnosis as gold standard sensitivity of 83% for MR-DWI and 26% for NCCT were calculated.[8]

In a retrospective study, 19 of 346 patients with initial negative MR-DWI findings were detected to have stroke and false negative results occurred more often in posterior circulation (11.9%) than anterior circulation (2.3%). The authors have concluded that, negative MR-DWI could not rule out acute stroke in posterior circulation stroke without cardioembolic risk factor.[16]

The diagnostic accuracy of MR-DWI in our study was in accordance with the previous studies. Stroke was not detected in any patient when MR-DWI was normal. MR-DWI may be a quick and valuable tool in patients with inconclusive neurological signs and symptoms. This technique may prevent unnecessary admission to hospital, and in this regard, it may be a cost effective strategy. Clinicians should be careful with the patients presenting to ED with inconclusive signs and symptoms that suggest a posterior circulation disorder. This study is distinguished from the previous studies by only including the patients without objective neu-

TABLE 2: Demographic properties of study participants.

		Stroke Present		Stroke Absent		p
		n	%	n	%	
Gender	Female	5	6.4%	29	37.2%	0.26
	Male	12	15.4%	32	41%	
		Mean ± Standard Deviation				
Age		54 ± 19.4		66 ± 12.7		0.02

TABLE 3: Detection of stroke with MR-DWI in different studies.

Study	Number of Patients, design	Sensitivity MR-DWI	Specificity MR-DWI	PPV MR-DWI	NPV MR-DWI
Mullins ME et al.[9]	691,retrospective	97	92	96	77
Fiebach J. et al.[10]	31, prospective	100	N/A	N/A	N/A
Fiebach JB. et al.*[11]	54, prospective	91.81	65.56	96.93	47.30
Urbach H.et al.°[12]	30, prospective	100.95	100.80	100.96	100.65
Langsberg MG et al.[13]	19, prospective	100	N/A	N/A	N/A
Gonzales RG et al.[4]	22, prospective	100	100	100	100
Barber PA et al.[14]	17, prospective	100	N/A	100	100
Saur D et al.[15]	45, prospective	93	N/A	N/A	N/A

*The first value is 'expert' reader and the second value is 'novice' reader.

° The first value is consensus interpretations and the second value is individual interpretations.

rological signs. MR-DWI may shorten time to diagnosis and it may have a positive effect on overcrowding in EDs and hospital wards.

This study because of its retrospective design may have several limitations. The 6 hours period after symptom onset may have been longer in some patients. The first imaging modality was NCCT, leading an advantage to MR-DWI. Residents and faculty members of Radiology were not blinded to clinical data but NCCT and MR-DWI were interpreted by two separate teams.[7]

In conclusion, MR-DWI is a quick and valuable imaging modality in the ED. The results of the test can be used in daily practice of busy EDs. The test can change the management strategy of NCCT negative patients with new stroke-like symptoms when a decision about patient treatment required additional information.

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