Transient Ischemic Attack: Which Determines Diffusion-Weighted Image Positivity?

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Aim of the study: Diffusion-weighted image (DWI) of magnetic resonance imaging (MRI) can reveal high signal lesion in up to 50% of transient ischemic attack (TIA) patients. However, it is not well-known which factors determine developing DWI positivity. In order to answer this question, we analyzed factors relevant to DWI positivity in TIA patients. *Methods:* We had 257 stroke patients at a university emergency/neurology wards. They were 140 men, 117 women, mean age 72 (45-88) years. Among them, 24 (9.3%) had TIA (14 men, 10 women, mean age 71 [58-82] years). All patients underwent a 1.5T MRI. In 24 TIA patients, we investigated the following parameters in relation with stroke maturation: ABCD2 score, smoking habits, blood profile, HbA1C, dyslipidemia, coagulation factors, carotid echography, electrocardiography, cardiac echography, chest X-ray, neurological symptom/signs, imaging, and recurrence of neurological symptom on follow-up. *Results:* In 24 TIA patients, 13 (54%) were DWI positive and 11 (46%) were DWI negative. After an extensive analysis, all parameters were not relevant to DWI positivity except for plasma osmolarity, i.e., plasma osmolarity in DWI positive cases (305.3 mOsm/l) is significantly higher than that in DWI negative cases (301.3 mOsm/l) ($P = .0064$). As for recurrence, 4 of 24 TIA patients recurred. They were 1 (9.0%) of 11 DWI negative cases and 3 (23.1%) of 13 DWI positive cases. Therefore, DWI positive cases recurred more frequently than DWI negative cases did, although it did not reach statistical significance. *Conclusions:* TIA with DWI positivity in our institute was 54%, closely associated with initial dehydration and might predict stroke recurrence.

Key Words: Transient ischemic attack—stroke—diffusion-weighted image—prognosis—osmolarity

Introduction

Transient ischemic attack (TIA) is defined as a vascular neurological syndrome in which symptoms resolve completely within 24 hours, and brain imaging finding is not included in the definition of TIA. More recently, diffusion-weighted image (DWI) of magnetic resonance imaging (MRI) can reveal high signal lesion in up to 50% of TIA patients.[1-6] In contrast, up to now, it is not well-known which factors determine developing DWI positivity.[1] In order to answer this question, we analyzed factors relevant to DWI positivity in TIA patients.

Methods

We had 257 stroke patients at a university emergency and neurology wards during 2008-2016. We performed an initial workup within 1 hour after hospital arrival, including standard neurological examination, blood sampling, chest X-ray, electrocardiogram, and a brain MRI.

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All patients underwent MRI examinations on a 1.5T Gyroscan (Philips, Best, the Netherlands), a 1.5T Optima MR450w scanner (GE Healthcare, Waukesha, WI, USA), or a 3T Skyra MRI system. In addition to DWI with thickness 4mm, gap .8 mm, we obtained T1-weighted, T2-weighted, Fluid Attenuated Inversion Recovery and T2 star or susceptibility-weighted images, MR angiography, and arterial spin labeling perfusion images. They were 140 men, 117 women, mean age 72 (45-88) years.

Among them, 24 (9.3%) had TIA (14 men, 10 women, mean age 71 [58-82] years). In 24 TIA patients, we investigated the following parameters in relation with DWI positivity: dyslipidemia (a serum total cholesterol level of <220 mg/dl, an high-density lipoprotein -cholesterol level of ≧40 mg/dl, an low-density lipoprotein -cholesterol level of <140 mg/dl, a triglyceride level of <150 mg/dl), ABCD[2] score (a stroke progression indicator, A [age, point 1: > 60 years]-B [blood pressure, point 1: systolic > 140 mmHg and/or diastolic >90 mmHg]-C [clinical features, point 2: hemiparesis, point 1: dysarthria]-D [duration, point 2: >60 min, point 1: <60 min],[diabetes, a fasting blood glucose level of <126 mg/dl, an HbA1c (NGSP) level of <6.5%, point 1]), in addition to their medications, smoking habits (current smoking or not), blood profile (including plasma osmolarity), coagulation factors (including d-dimer), carotid echography (plaque score), electrocardiography (including atrial fibrillation), cardiac echography (including ejection fraction), chest X-ray, neurological symptom/signs, imaging (interval [hours] between occurrence of neurological symptom and image acquisition, location, vascular supply and volume of lesion on MRI), and recurrence of neurological symptom on follow-up (mean 4.0 years [1-9 years]). Statistics were analyzed by non-parametric Wilcoxon signed-rank test.

Results

In 24 TIA patients, 13 (54%) were DWI positive and 11 (46%) were DWI negative. After an extensive analysis, the below parameters were not statistically correlated to the DWI positivity, i.e., presence of atrial fibrillation, myocardial infarction, congestive heart failure; plaque score of carotid ultrasound; Brinkman index as smoking habit; dyslipidemia (high-density lipoprotein, low density-lipoprotein, triglyceride), HbA1C as diabetes; body mass index as obesity; kidney function (blood urea nitrogen, creatinine, estimated glomerular filtration rate); d-dimer; ABCD[2] score (total score, A, B,C, D1, D2); interval between arrival to MRI; and therapies (Table 1). In contrast, only plasma osmolarity in DWI positive cases (305.3 mOsm/l) is significantly higher than that in DWI negative cases (301.3 mOsm/l) ($P = .0064$) (Table 1, Fig 1). As for recurrence, 4 of 24 TIA patients recurred. They were 1 (9.0%) of 11 DWI negative cases and 3 (23.1%) of 13 DWI positive cases. Therefore, DWI positive cases recurred more frequently than DWI negative cases did, although it did not reach statistical significance.

Discussion

Previously it is not well-known which factors determine DWI positivity. Among these, Engelter et al.[1] found factors relevant to DWI positivity, e.g., larger lesion size and severer apparent diffusion coefficient decrease than DWI negative cases; few in infratentorial lesion; more in patients whose TIA symptom greater than 4 hours; but still detectable in patients whose TIA symptom less than 1 minute. Shono et al.[6] reported that DWI positivity is not easily detectable within 2 hours after the onset of TIA symptom. Uno et al.[4] reported that, if MRI is performed after the offset of TIA symptom, DWI positivity is highly detectable at 0-1 hour (30.8%). However, we did not replicate any of these findings. For the first time to our knowledge, we found that plasma osmolarity in DWI positive cases is significantly higher than that in DWI negative cases. It is recognized that dehydration in the elderly causes worsening of cognition and locomotion.[7] Previously, few literatures are available suggesting that dehydration correlates with the occurrence of atherosclerotic stroke. However, in high-risk groups (atrial fibrillation,[8] Crohn's disease,[9] etc.), dehydration correlates with the occurrence of stroke. In light of the present study results, dehydration might also trigger the development of DWI positivity. Recent metabolomics study also suggested that not only dehydration, but also creatinine, threoninyl-threonine, N-acetyl-glucosamine, lysophosphatidic acid, and cholesterol-related molecules related with DWI positivity.[10] The underlying mechanism for producing DWI positivity by these molecules awaits further studies. Previously it is reported that DWI positivity predicts future risk of recurrent stroke.[6,11,12] Our finding that DWI positive cases (23.1%) recurred more than DWI negative cases did (9%) seemed to corroborate these findings, although our finding did not reach statistical significance. Our study has limitations including a limited number of TIA cases, and no control. Nevertheless, our study results may facilitate future studies involving a larger sample size in TIA patients. Whereas detection rate of DWI positivity in TIA is still not high at this moment, newer DWI technology[13] with a combination of perfusion[14] and/or tensor imaging[15] might increase detection rate of stroke which is highly warranted.

Taken together, TIA with DWI positivity in our institute was 54%, closely associated with initial dehydration and might predict stroke recurrence.

Table 1. *Clinical and laboratory demographic data at admission in TIA patients with positive/negative DWI MRI imaging*

MRI	Age	Sex	Premorbid systemic status														ABCD score on admission						Interval between arrival to MRI (h)	Therapy
DWI			Atrial fibrillation	Myocardial infarction	Congestive heart failure	Carotid ultrasound plaque score	Smoking Brinkman index	Dyslipidemia			Diabetes HbA1c	Body mass index	Kidney function			d-dimer	Plasma osmorality	Total	A	B	C	D1	D2		
								HDL	LDL	TG			BUN	Cr	eGFR										
Negative	42	M	–	–	–	1.5	1000	34	100	388	5.4	30.1	23	1.25	52	.55	304.3	4	0	1	0	2	1	2	Ozagrel
	55	M	–	–	–	2.3	600	33	123	97	7.9	30	15	.81	77	.55	301.1	6	0	1	2	2	1	6	Aspirin
	57	M	–	–	–	2.9	555	48	43	221	7.7	23	12.1	.9	68	.5	296.5	4	0	1	2	0	1	16	Ozagrel
	70	M	–	–	–	16.6	800	40	166	165	6.3	24	10.3	1.09	53	.66	304.9	3	1	1	1	0	0	7	Ozagrel
	70	F	–	–	–	4.62	0	59	86	139	5.6	22.6	16.2	.65	68		301.7	6	1	1	2	2	0	5	Ozagrel
	71	M	–	–	–	15	1000	47	102	1055	7.1	24.1	14.8	.79	74	1.58	297.1	5	1	0	2	1	1	12	Aspirin+ Ozagrel
	72	F	–	–	–	3.1	500	52	107	123	5.6	21.7	12.7	.56	79	.5	303.4	4	1	1	0	2	0	5	Argatroban
	77	F	–	–	–	5	0	68	137	127	6.3	21	10.1	.67	64	.5	301.1	4	1	0	1	2	0	2	Ozagrel
	79	M	+	–	–	2.9	0	49	89	195	6.3	21.4	20.7	.94	59	.86	302.9	4	1	1	1	1	0	2	Apixaban
	82	M	–	–	+	10.3	1000	35	137	95	5.1	24.5	16.5	1.21	44	.86	298.8	5	1	1	2	1	0	5	Ozagrel
	86	M	+	–	+	14.8	0	49	88	55	5.6	22	14.1	.72	77	0.5	301.9	5	1	1	1	1	1	3	Dabigatran
Average	69					7.2	495.9	46.7	107.1	241.8	6.3	24.0	15.0	.9	65.0	.7	301.2*	4.5	.7	.8	1.3	1.3	.5	5.9	
SD	13					5.8	430.4	10.8	32.9	284.0	.9	3.2	4.0	.2	11.7	.3	2.8	.9	.5	.4	.8	.8	0.5	4.4	
Positive	56	M	+	–	–	0	0	54	140	180	5.6	22.3	14.3	.87	71	.5	305	2	0	0	1	1	0	4	Edoxaban
	56	M	–	–	–	9.8	1380	47	125	94	7	25.4	18.8	.59	109	.76	296	5	0	1	1	2	1	12	Ozagrel
	65	M	+	–	+	17	960	47	144	187	6.6	30.8	13.2	.73	83	1.12	301.6	4	1	1	1	1	0	2	Apixaban
	65	M	–	–	–	6.7	800	49	134	151	6.4	23.8	16.5	1.08	54	.5	303	5	1	1	1	1	1	6	Aspirin
	65	F	–	–	–	1.19	0	73	180	107	6	20.8	16.7	.72	62	.5	308.4	6	1	1	2	2	0	7	Ozagrel
	72	F	–	–	–	1.2	0	58	160	70	6.3	–	19.8	.57	78	.59	299.1	6	1	1	2	2	0	3	Ozagrel
	74	M	–	–	–	18.1	1000	32	129	121	6.4	17.7	22.7	.83	69	1.19	304.9	5	1	0	2	2	0	12	Ozagrel
	79	M	–	–	–	17.9	0	62	89	493	6.1	23.9	24.3	2.05	25	1.49	306.9	7	1	1	2	2	1	2	Ozagrel+ Clopidogrel
	80	M	+	–	+	15	0	33	90	217	5.9	27.2	55.4	2.91	17	5.3	313.7	5	1	0	2	2	0	1	Wafarin+ Heparin
	80	F	+	–	+	15.7	0	62	107	71	6.6	18.3	18	.64	66	2.58	309	4	1	1	0	1	1	3	Dabigatran
	81	M	–	–	–	4.1	600	45	74	100	5.4	24.8	10.8	.74	76	.5	302.9	3	1	0	0	2	0	3	Ozagrel
	81	F	–	–	–	13.7	0	53	126	146	5.5	23.1	12	.59	72	.69	306.3	6	1	1	2	2	0	4	Ozagrel
	87	F	–	–	–	5.6	0	88	73	58	5.7	–	11.2	.9	45	5.82	300.2	6	1	1	1	1	0	12	Aspirin
Average	72					9.7	364.6	54.1	120.8	153.5	6.1	23.5	19.5	1.0	63.6	1.7	304.4*	4.9	.8	.7	1.4	1.7	.3	5.5	
SD	10					6.9	508.1	15.3	32.7	113.2	.5	3.8	11.6	.7	24.3	1.8	4.7	1.4	.4	.5	.8	.5	.5	4.1	

Abbreviations: BUN, blood urea nitrogen; Cr, creatinine; DWI, diffusion-weighted image; eGFR, estimated glomerular filtration rate; HDL, high-density lipoprotein; LDL, low-density lipoprotein; MRI, magnetic resonance imaging; SD, standard deviation; TG, triglyceride.

Statistics were analyzed by nonparametric Wilcoxon signed-rank test.

*$P < .05$.

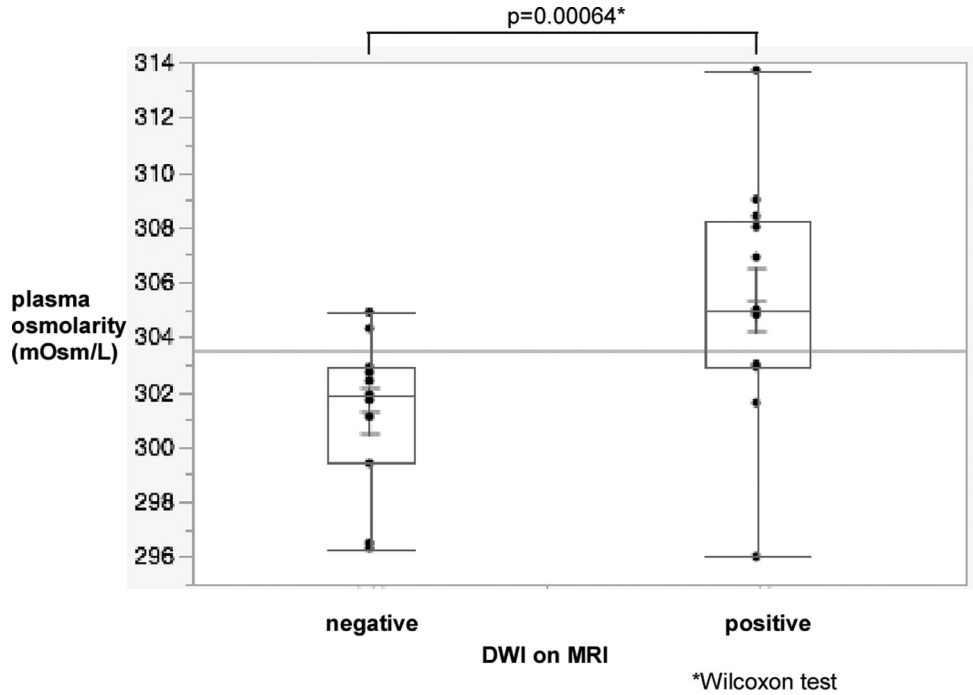

Figure 1. *Plasma osmolarity at admission in TIA patients with positive/ negative DWI MRI imaging. Statistics were analyzed by nonparametric Wilcoxon signed-rank test. Abbreviations: DW, diffusion-weighted image; MRI, magnetic resonance imaging; TIA, transient ischemic attack.*

Authors Contribution

Yosuke Aiba has a role in: acquisition of subjects and/or data, and analysis and interpretation of data.

Ryuji Sakakibara has a role in: study concept and design, acquisition of subjects and/or data, analysis and interpretation of data, and preparation of manuscript.

Fuyuki Tateno has a role in: acquisition of subjects and/or data.

Tsuyoshi Ogata has a role in: acquisition of subjects and/or data.

Takeki Nagao has a role in: acquisition of subjects and/or data.

Hitoshi Terada has a role in: acquisition of subjects and/or data.

Tsutomu Inaoka has a role in: acquisition of subjects and/or data.

Tomoya Nakatsuka has a role in: acquisition of subjects and/or data.

Conflict of Interest

None of the authors have conflict of interest.

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