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Research report

The degree of leukoaraiosis predicts clinical outcomes and prognosis in patients with middle cerebral artery occlusion after intravenous thrombolysis

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ABSTRACT

Leukoaraiosis (LA) is common in elderly patients with ischemic stroke on magnetic resonance imaging. In this study, we investigate whether the degree of LA is associated with clinical outcomes and prognosis of patients with middle cerebral artery occlusion following intravenous thrombolytic. Ninety-seven patients were recruited and divided into three groups based on the degree of LA (no, mild and moderate to severe LA) by the Fazekas scale. Clinical outcomes, recurrent stroke, Fugl-Meyer rating scale (FMS) and complications of intravenous thrombolysis were assessed. The association between the degree of LA and functional outcomes was analyzed by multivariable logistic regression model. Patients enrolled were divided into three groups: 26 patients with no LA, 43 patients with mild LA and 28 patients with moderate to severe LA. Impressively, the patients with mild LA were better in early neurological recovery and 90-day FMS score than patients in the other two groups. Multivariate logistic analysis revealed that moderate to severe LA was an independent predictor of poor functional outcome (OR: 10.482; 95% CI: 1.442–76.181; $P = .020$). Moreover, the patients with moderate to severe LA have a higher rate of hemorrhagic transformation and recurrent stroke as compared with two other groups during 90-day follow-up. Different degrees of LA differentially affect clinical outcome and prognosis in patients with middle cerebral artery occlusion following intravenous thrombolytic. Moderate to severe LA is a risk factor of poor prognosis. Mild LA is associated with early neurological recovery and good motor functional outcome.

1. Introduction

Intravenous thrombolysis (IVT) with recombinant tissue plasminogen activator (rt-PA) is the first choice for acute ischemic stroke (AIS) within 4.5 h after onset (Tsivgoulis et al., 2017). Unfortunately, not all patients with AIS benefit from IVT, which may be relevant to the destruction of rt-PA on blood-brain barrier (BBB), increasing brain injury or hemorrhagic transformation (HT), thereby leading to poor function outcome (Avsenik et al., 2015; Simao et al., 2017). Previous studies showed that leukoaraiosis (LA), which is characterized by periventricular hyperintensity and deep white matter hyperintensity of chronic ischemic on MRI scanning, might be also associated with dysfunction of BBB (Bridges et al., 2014; Edrissi et al., 2016; Pantoni, 2010). Thus, we speculated that rt-PA may affect the prognosis of AIS patients with LA.

However, LA is a progressive disease affected by many risk factors, suggesting that different degrees of LA may reflect different pathogenesis and influence differentially the prognosis of the patients. There is evidence that moderate to severe LA may be associated with severe intracranial vascular lesions leading to dysfunction of small vessels. Also, previous studies reported that carotid artery stenosis is associated with LA lesions, especially in the territory of middle cerebral artery (MCA) (Ben-Assayag et al., 2012; Demirtas et al., 2013). In contrast, mild LA may suggest better collateral circulation compensation, being a marker of chronic ischemia (Giurgiutiu et al., 2015). Based on these studies, the objective of this study was to further evaluate the effect of different degrees of LA on clinical outcomes and relevant complications in patients with middle cerebral artery (MCA) occlusion following IVT.

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2. Results

2.1. Patients

Ninety-seven patients were eventually enrolled into this study according to inclusion criteria and exclusion criteria. Their mean age was 66.6 ± 9.1 years and 68 patients (70.1%) were male. Following IVT, 47 patients (48.5%) exhibited early neurological recovery. HT and sICH were observed in 16 (16.5%) patients and 9 (9.3%) patients, respectively. During 90-day follow-up after the onset, 19 patients (19.6%) had recurrent stroke. Data are presented in Table 1.

2.2. Baseline characteristics

Based on the Fazekas scale, the enrolled 97 patients with AIS were divided into three groups: no LA group, including 26 patients (26.8%); mild LA group, including 43 patients (44.3%); moderate to severe LA group, including 28 patients (28.9%). Baseline characteristics of these groups are summarized in Table 2. Among three groups, there were no significant differences in age, sex, fasting plasma glucose, stroke risk factors (hypertension, diabetes mellitus, hyperlipidemia, coronary artery disease, arterial fibrillation, smoking and drinking), time from onset to thrombolysis, baseline NIHSS scores and FMS scores, as well as sICH ($p > .05$). However, there were significant differences in early neurological recovery ($F = 16.402$, $P < .001$; Fig. 1), HT ($F = 10.587$, $P = .005$), recurrent stroke ($F = 9.697$, $P = .008$) and 90 days FMS score ($x^2 = 11.466$, $P < .001$) among three groups (Table 2).

2.3. Association between the degrees of LA and clinical outcomes

As shown in Table 2, the percentage of the mild LA group was higher in early neurological recovery than that of the no LA group or that of the moderate to severe LA group (69.8% vs 42.3%; $P = .024$; 69.8% vs 21.4%; $P < .001$; the multiple test with Bonferroni correction). In contrast, the incidence rate of HT in the moderate to severe LA group was higher than that in the no LA group or in the mild LA group (35.7% vs 7.7%; $P = .013$; 35.7% vs 9.3%; $P = .006$; the multiple test with Bonferroni correction). Moreover, as compared to the no LA group or the mild group, the moderate to severe LA group displayed the highest rate of recurrence stroke

Table 1
Characteristics of the study population.

Characteristics	
Age (years, mean ± SD)	66.6 ± 9.1
Male, N (%)	68 (70.1)
Initial NIHSS (mean ± SD)	11.1 ± 5.8
Initial FMS (mean ± SD)	76.4 ± 17.7
Risk factors	
Hypertension, N (%)	73 (75.3)
Diabetes mellitus, N (%)	35 (36.1)
Hyperlipidemia, N (%)	45 (46.4)
Coronary artery disease, N (%)	11 (11.3)
Arterial fibrillation, N (%)	19 (19.6)
Smoking, N (%)	43 (44.3)
Drinking, N (%)	27 (27.8)
Time to thrombolysis	
<3.0 h	50 (51.5)
3.0–4.5 h	47 (48.5)
Clinical variables	
Early neurological improvement, N (%)	47 (48.5)
Hemorrhagic transformation, N (%)	16 (16.5)
Symptomatic intracranial hemorrhage, N (%)	9 (9.3)
90d recurrence of stroke, N (%)	19 (19.6)
90d FMS (mean ± SD)	82.8 ± 2.9
LA severity, N (%)	
0 absent	28 (28.9)
1–2 mild	43 (44.3)
3–6 moderate to severe	26 (26.8)

LA: leukoaraiosis; SD: standard deviation; NIHSS: National Institutes of Health Stroke Scale; FMS: Fugl-Meyer rating scale.

Table 2
Baseline characteristics of patients stratified by the degree of LA.

Characteristics	None LA (n = 26)	Mild LA (n = 43)	Moderate to severe LA (n = 28)	F/x^2	P
Age (years, mean ± SD)	65.4 ± 10.4	65.5 ± 6.4	69.4 ± 8.4	2.327	0.103[b]
Male, N (%)	20 (76.9)	33 (76.7)	15 (53.6)	5.133	0.077
Baseline NIHSS score (mean ± SD)	10.7 ± 6.5	10.9 ± 5.3	11.7 ± 6.0	0.240	0.787[b]
Initial FMS score (mean ± SD)	80.5 ± 17.9	76.5 ± 15.1	72.4 ± 20.8	1.401	0.251[b]
Risk factors					
Hypertension, N (%)	20 (76.9)	30 (69.8)	23 (82.1)	1.448	0.485
Diabetes mellitus, N (%)	7 (26.9)	14 (32.6)	14 (50.0)	3.529	0.171
Hyperlipidemia, N (%)	10 (38.5)	25 (58.1)	10 (35.7)	4.327	0.115
Coronary artery disease, N (%)	2 (7.7)	6 (14.0)	3 (10.7)	0.668	0.716
Arterial fibrillation, N (%)	3 (11.5)	11 (25.6)	5 (21.4)	2.103	0.349
Smoking, N (%)	12 (46.2)	22 (51.2)	9 (32.1)	2.534	0.282
Drinking, N (%)	7 (26.9)	15 (34.9)	5 (17.9)	2.462	0.292
Glucose (mean ± SD, mg/ml)	6.9 ± 2.9	8.0 ± 3.0	6.3 ± 2.7	0.834	0.364[b]
Time to thrombolysis				1.305	0.521
<3.0 h, N (%)	15 (57.7)	23 (53.5)	12 (42.9)		
3.0–4.5 h, N (%)	11 (42.3)	20 (46.5)	16 (57.1)		
Clinical variables					
Early neurological recovery, N (%)	11 (42.3)	30 (69.8)[a]	6 (21.4)	16.402	<0.001
HT, N (%)	2 (7.7)	4 (9.3)	10 (35.7)[c]	10.587	0.005
sICH, N (%)	1 (3.8)	3 (7.0)	5 (17.9)	3.630	0.163
Recurrence of stroke, N (%)	3 (11.5)	5 (11.6)	11 (39.3)[c]	9.697	0.008
90d FMS score (mean ± SD)	84.4 ± 22.4	95.3 ± 6.1[a]	69.8 ± 33.9[c]	11.466	<0.001[b]

LA: leukoaraiosis; SD: standard deviation; NIHSS: National Institutes of Health Stroke Scale; FMS: Fugl-Meyer rating scale; HT: hemorrhagic transformation; sICH: symptomatic intracranial hemorrhage.
[a,c] $P < .05$.
[a] Mild LA versus no LA or moderate to severe LA.
[b] One-way ANOVA value, others Chi-square value.
[c] Moderate to severe LA versus mild LA or no LA (multiple tests with Bonferroni correction or LSD t test).