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Pre-stroke glycemic control is associated with early neurologic deterioration in acute atrial fibrillation-related ischemic stroke

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ABSTRACT

Background: It has been suggested that AF-related ischemic stroke (IS) that is accompanied by atherosclerotic burden have poorer outcomes. The aim of this study was to investigate the importance of pre-stroke glycemic control (PSGC) on the early neurologic deterioration (END) of patients with acute AF-related IS.

Methods: We retrospectively recruited 121 patients with AF-related IS who also had Diabetes mellitus (DM). The HbA1C level was measured in all subjects. END was defined as an increase in the National Institute of Health Stroke Scale (NIHSS) score of 4 NIHSS points within 7 days of symptom onset compared to the initial NIHSS score.

Results: In this study, 20.7% (25 patients) were classified as having a poor PSGC status with a HbA1C level above 8.0%. In the univariate analysis, a poor PSGC status ($p < 0.01$), smoking ($p = 0.01$), severe neurologic deficits at admission ($p = 0.01$), and a larger size of ischemic lesions on DWI ($p < 0.01$) were associated with the occurrence of END. In the multivariate model, a poor PSGC status ($p = 0.02$) and larger size of ischemic lesions on MRI ($p < 0.01$) were independent predictors of END in acute AF-related IS.

Conclusion: The HbA1c level upon admission was independently associated with significant prediction of END in acute AF-related IS.

1. Introduction

Atrial fibrillation (AF) is the most common cause of cardioembolism (CE), [1] accounting for 77% of the high-risk cardiac sources of embolism in ischemic stroke (IS). AF-related IS exhibits higher recurrence and mortality than other IS types [2].

Unlike other etiologies of CE, AF is significantly influenced by the presence of systemic atherosclerosis, which initiates ischemic events. Recently, the presence of carotid plaques has been associated with an increased risk of ischemic stroke in individuals with AF [3]. Additionally, several studies reported an increase in CHADS2/CHA2DS2-VASc scores, indicating that the presence of systemic atherosclerosis was related to high mortality and poor outcomes in patients who experienced AF-related IS [4,5]. It suggested that the atherosclerotic burden might contribute to the progression of neuronal damage in acute AF-related IS. The presence of diabetes mellitus is an important factor in the progression of atherosclerosis. Several studies have demonstrated that a poor pre-stroke glycemic control (PSGC) state is associated with short- [6,7] and long-term outcomes after acute IS [8,9], regardless of the subtype [10].

Early neurologic deterioration (END) is a significant event encountered in acute IS, and the predictive factors of END have not yet been fully elucidated [11,12]. Recently, a poor PSGC state in patients with acute ischemic stroke has been shown to be associated with the occurrence of END [6,7]. The aforementioned studies were primarily performed in non-cardioembolic IS, such as those affecting the penetrating artery or brainstem infarctions. However, until now, it has been unclear whether the PSGC status might be a critical predictor of the presence of END in AF-related IS.

The aim of this study was to investigate the importance of PSGC in the early neurologic deterioration of patients with acute AF-related IS.

2. Methods

From January 2013 to December 2015, we retrospectively recruited AIS patients (within 24 h after their ischemic events) who were registered in the Dong-A University Stroke registry. In this study, we selected patients with CE based on TOAST classification [13] with MRI

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Table 1
Baseline characteristics of patients according to level of HbA1C.

		Total	HbA1C			p-Value
			6.0–6.9	7.0–7.9	≥ 8.0	
Total		121	73 (60.3)	23 (19.0)	25 (21.0)	
Sex	Male	61 (50.4)	31 (51.0)	12 (20.0)	18 (30.0)	0.04
	Female	60 (50.0)	42 (70.0)	11 (18.3)	7 (11.7)	
Age (yr)	Mean ± std	73.3 ± 8.6	74.4 ± 9.0	71.2 ± 7.5	72.2 ± 8.0	0.23
	Median (IQR)	74.0 (51.0–92.0)	75.0 (51.0–92.0)	73.0 (54.0–83.0)	73.0 (58.0–86.0)	0.20
	≤ 69	40 (33.1)	20 (50.0)	11 (28.0)	9 (23.0)	0.40
	70–79	54 (45.0)	34 (63.0)	8 (15.0)	12 (22.2)	
	≥ 80	27 (22.3)	19 (70.4)	4 (15.0)	4 (15.0)	
Hypertension	No	28 (23.1)	17 (61.0)	4 (14.3)	7 (25.0)	0.69
	Yes	93 (77.0)	56 (60.2)	19 (20.4)	18 (19.4)	
Smoking	No	107 (88.4)	67 (63.0)	20 (19.0)	20 (19.0)	0.27
	Yes	14 (12.0)	6 (43.0)	3 (21.4)	5 (36.0)	
Old_CAD	No	107 (88.4)	64 (60.0)	19 (18.0)	24 (22.4)	0.33
	Yes	14 (12.0)	9 (64.3)	4 (29.0)	1 (7.1)	
Old CVA	No	112 (93.0)	66 (59.0)	21 (19.0)	25 (22.3)	0.28
	Yes	9 (7.4)	7 (78.0)	2 (22.2)	0 (0.0)	
t-PA	No	80 (66.1)	45 (56.3)	15 (19.0)	20 (25.0)	0.25
	Yes	41 (34.0)	28 (68.3)	8 (19.5)	5 (12.2)	
Initial BP	Mean ± std	131.8 ± 21.4	133.0 ± 20.7	128.7 ± 24.6	131.2 ± 21.1	0.70
	Median (IQR)	130.0 (80.0–190.0)	130.0 (100.0–190.0)	120.0 (100.0–190.0)	130.0 (80.0–190.0)	
Initial NIHSS (quartile)	Mean ± std	9.38 ± 7.42	8.63 ± 6.61	9.91 ± 8.10	11.08 ± 8.89	0.34
	Median (IQR)	8.0 (0.0–28.0)	7.0 (0.0–26.0)	8.0 (0.0–25.0)	12.0 (0.0–28.0)	0.55
	≤ 2	28 (23.1)	15 (54.0)	7 (25.0)	6 (21.4)	0.41
	3–8	34 (28.1)	23 (68.0)	5 (15.0)	6 (18.0)	
	9–14	27 (22.3)	20 (74.1)	3 (11.1)	4 (15.0)	
	15–28	32 (26.4)	15 (47.0)	8 (25.0)	9 (28.1)	
Serum glucose (mg/dl) (quartile)	Mean ± std	158.83 ± 60.80	142.47 ± 45.01	159.78 ± 50.95	205.72 ± 83.19	< 0.01
	Median (IQR)	143.0 (66.0–461.0)	134.0 (77.0–272.0)	143.0 (66.0–260.0)	208.0 (73.0–461.0)	< 0.01
	≤ 117	31 (26.0)	23 (74.2)	4 (13.0)	4 (13.0)	< 0.01
	> 117–143	30 (25.0)	20 (67.0)	8 (27.0)	2 (7.0)	
	> 143–193	30 (25.0)	21 (70.0)	4 (13.3)	5 (17.0)	
	> 193	30 (25.0)	9 (30.0)	7 (23.3)	14 (47.0)	
LDL (mg/dl) (quartile)	Mean ± std	99.98 ± 36.08	102.56 ± 37.38	88.13 ± 25.94	103.46 ± 39.27	0.22
	Median (IQR)	99.5 (31.0–218.0)	102.0 (31.0–218.0)	81.0 (41.0–129.0)	96.5 (35.0–194.0)	0.31
	≤ 75	29 (24.2)	18 (62.1)	8 (28.0)	3 (10.3)	0.29
	> 75–99	31 (26.0)	15 (48.4)	6 (19.4)	10 (32.3)	
	> 99–119	31 (26.0)	20 (65.0)	6 (19.4)	5 (16.1)	
	> 199	29 (24.2)	20 (69.0)	3 (10.3)	6 (21.0)	
New AF	No	49 (40.5)	34 (69.4)	6 (12.2)	9 (18.4)	0.47
	Yes	72 (59.5)	39 (54.2)	17 (23.6)	16 (22.2)	
END	No	105 (87.0)	68 (65.0)	21 (20.0)	16 (15.2)	< 0.01
	Yes	16 (13.2)	5 (31.3)	2 (13.0)	9 (56.3)	
Size of DWI (CC) (quartile)	Mean ± std	40.31 ± 59.71	32.12 ± 51.34	34.38 ± 56.57	69.70 ± 76.47	0.02
	Median (IQR)	11.3 (0.0–270.0)	8.8 (0.0–241.4)	9.5 (0.0–200.0)	55.4 (0.2–270.0)	0.02
	≤ 2.61	31 (26.0)	21 (68.0)	6 (19.4)	4 (13.0)	0.18
	> 2.61–11.28	30 (25.0)	20 (67.0)	7 (23.3)	3 (10.0)	
	> 11.29–60.00	31 (26.0)	19 (61.3)	5 (16.1)	7 (23.0)	
	> 60.00	29 (24.0)	13 (45.0)	5 (17.2)	11 (38.0)	

Old CAD: previous history of coronary artery diseases, old CVA - previous history of cerebrovascular accident, initial BP - initial measurement of blood pressure at emergency room, LDL - low density lipoprotein, new AF - newly diagnosed atrial fibrillation after admission, END - early neurologic deterioration, DWI - diffusion weighted images.

screening. Additionally, we excluded patients with valvular heart disease among those patients with CE. For the purpose of the study, only the patients with an established diagnosis of DM at the time of hospital admission were included; DM was defined according to patients' self-reported histories or based on the use of a hypoglycemic drug or insulin.

For each patient, we recorded their age, sex, and the presence of vascular risk factors. A quantitative determination of plasma HbA1c (%) using high-performance liquid chromatography was performed for all patients as a PSGC parameter.

The stroke mechanism categories were classified using acute stroke treatment classification of the modified Trial of Org 10,172 in Acute Stroke Treatment. The local ethics review board approved this study.

Stroke severity was assessed by the National Institutes of Health Stroke Scale (NIHSS), which was performed in the emergency room. We measured NIHSS at 24 h, 72 h, and 7 days after admission and at discharge. Early neurological worsening was defined as an increase in the NIHSS score of ≥ 4 NIHSS points within 7 days of symptom onset compared to the initial NIHSS score. In patients with END, we took follow up images, including brain CT or MRI, to identify their causes.

2.1. MR imaging and analysis

MRI (1.5 T, Signa Echospeed Superconducting Imaging System; General Electric Medical Systems, Milwaukee, Wl, USA) images included T1, axial fluid-attenuated inversion recovery (FLAIR), three-dimensional time-of-flight MR angiography, axial diffusion-weighted imaging (DWI), and axial perfusion-weighted imaging (PWI). DWI was performed using echo-planar imaging (EPI) techniques. The edge of the DWI abnormality was visually identified using the trace of the diffusion coefficient, and regions of interest (ROIs) were outlined using a pixel-wise method.