Original Article

Significance of Multiple Acute Ischemic Lesions on Initial Diffusion-weighted Imaging in Stroke Patients and Relation of Toast Classification

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Abstract

Background: It is important to know whether or not the stroke risk factors and etiologies of patients with multiple acute infarcts are different to those of patients with a single acute infarct. **Aim:** The frequency of multiple acute infarct was investigated in ischemic stroke patients and a comparison was made of the characteristics of stroke patients with and without multiple acute infarct. **Patients and Methods:** We reviewed the clinical records of 988 ischemic stroke patients who were admitted within 1 week of the onset of stroke and diffusion-weighted imaging (DWI) was performed on first presentation. The clinical characteristics, laboratory, and imaging results were noted from the patient records. According to the DWI findings, the patients were separated into three groups as those with a single acute infarct in a single vascular territory (SI group), those with multiple acute infarcts in a single vascular territory (SMI group) and those with multiple acute infarcts in multiple vascular (MMI group) territories. The frequency of multiple acute infarcts was investigated, and a comparison was made of the characteristics of stroke patients with and without multiple acute infarcts. **Results:** The SMI group included 119 (12%) patients and the MMI group 126 (12.8%). The most common mechanisms of multiple acute infarcts are large artery atherosclerosis and cardiac origin emboli. Moreover, the risk factors most determined were hypertension, diabetes mellitus, and hyperlipidemia in the MMI group. **Conclusion:** No difference was determined between the groups in respect of stroke etiology and risk factors.

Keywords: Acute ischemic stroke, diffusion-weighted imaging, multiple vascular territory, single vascular territory

Introduction

In a proportion of ischemic stroke patients, the presence of more than one acute infarct is determined on diffusion-weighted imaging (DWI). It is important to know risk factors and etiologies of these patients whom with a single or multiple acute infarct in the selection of treatment in stroke patients. Antithrombotic agents are the mainstay of pharmacological modification of recurrence risk and include acetylsalicylic acid or clopidogrel. Oral anticoagulants have an established role in preventing recurrence among patients with cardioembolic infarcts, especially nonvalvular atrial fibrillation (AF).[1] In addition to primary prevention, part of the burden is potentially changeable with effective secondary prevention. It is important to select the appropriate drug and modifying patients' life according to the risk factors.

Multiple acute infarcts are generally thought to originate from large arteries or cardiac emboli and therefore, both the etiology and whether or not there are different risk factors from patients with single acute infarct are matters of debate.[2-10] In this study, the frequency of multiple acute infarct was investigated in ischemic stroke patients and a comparison was made of the characteristics of stroke patients with and without multiple acute infarct.

Patients and Method

Patients characteristics

We reviewed the clinical records of 988 ischemic stroke patients who were admitted within 1 week of the onset of

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stroke, and DWI was performed on first presentation between January 2012 and May 2015. The patients with hemorrhagic stroke, subakut, chornic, or watershed infarct on DWI sequence of magnetic resonance imaging (MRI) were excluded from the study.

The clinical characteristics, laboratory, and imaging results were noted from the patient records. Vascular risk factors were recorded as hypertension (HT), diabetes mellitus (DM), hyperlipidemia (HL), cardiac arrythmia, coronary artery disease (CAD), a history of stroke, malignancy, and chronic renal disease (CRD). HT was defined as previous use of antihypertensive medication or repeated blood pressure measurements of ≥140/90 mmHg. DM was defined as previous use of antidiabetic medication or fasting blood sugar of ≥126 mg/dl. HL was defined as previous use of lipid-lowering medication or overnight fasting cholesterol level of ≥220 mg/dl or low-density lipoprotein cholesterol of ≥140 mg/dl.[11]

The results were recorded of the tests evaluated with define the stroke etiology in the patients. Initial etiologic parameters as hemogram, sedimentation, urea, creatinine, glucose, transaminase, and lipid levels were studied in our hospital laboratory and ECG was evaluated for all of the patients. With the exception of one patient, transthoracic echocardiography (TTE) was assessed by the cardiologists to all the patients. Carotid stenosis wasevaluated by duplex sonography except three patients and MR angiography measured by NASCET method. Computed tomography (CT) angiography (40.6%) was also performed if MRI and Doppler results were discordant. Transoesophageal echocardiography (TEE) (2.53%) was assessed by the cardiologists and the prothrombotic profile was examined (protein C, protein S, antithrombin III, lupus anticoagulant, anticardiolipin antibodies, etc.,) to selected patients, most of those aged below 50 years.

Stroke severity was assessed using the National Institutes of Health Stroke Scale (NIHSS) score at admission. Stroke subtypes were classified according to the Trial of Org 10172 in Acute Stroke Treatment (TOAST) classification as large artery atherosclerosis (LAA), cardioembolism (CE), small vessel occlusion (SVO), stroke of other determined etiology, and stroke of undetermined etiology.[12]

Imaging analysis

The DWI was evaluated including apparent diffusion coefficient (ADC) map to all the patients within the first 7 days of the onset of ischemic stroke. DWI was performed in 153 patients within <6 h of symptom onset, in 672 patients within 7–24 h and in 163 after >24 h. Acute infarct was defined as region with increased signal intensity on DWI accompanied by decreased signal on corresponding ADC maps. Vascular territories were defined as two anterior circulation (left and right internal carotid artery) and one posterior circulation (vertebrobasilar system).[2,6,13] According to the DWI findings, the patients were separated into three groups as those with a single acute infarct in a single vascular territory (SI group), those with multiple acute infarcts in a single vascular territory (SMI group) and those with multiple acute infarcts in multiple vascular territories (MMI group) [Figures 1-3].[10] The SMI group included patients with multiple acute infarcts in unilateral anterior circulation or posterior circulation. The MMI group included patients with multiple acute infarcts in bilateral anterior circulation, unilateral anterior and posterior circulation, and bilateral anterior and posterior circulation. The comparison was made between the groups of etiology and risk factors. Multiple infarcts resulting from vascular variations were not considered as multiple infarcts. Patients with normal DWI and those with water-shed infarct were not included in the study. We performed the study after obtaining the approval of local Ethics Committee.

Statistical analysis

Statistical analysis was performed using a commercially available software package (PASW version 18.0;SPSS Inc., Chicago, III, USA). Standard deviation, median, minimum-maximum ratios, and frequency values were used in descriptive statistics of the data. Categorical variables were compared with χ^2 test. The mean difference significance was verified using the Student's *t*-test for two groups and the analysis of variance (ANOVA) test for three or more groups. The consistency of the distribution was verified using the Mann–Whitney U-test for groups and the Kruskal–Wallis test for skewed distributions. Multiple comparisons were made based on *post hoc* test results for variance analysis (ANOVA). Results were considered to be statistically significant at $P < 0.05$ level and statistically insignificant at $P > 0.05$ level in 95% confidence interval.

Results

A total of 988 acute ischemic stroke patients were included in this study. The patients comprised 527 (53.3%) males and 461 (46.7%) females with a mean age of 68.6 ± 12.3 years (range, 22–95 years). The SI group included 743 (75.2%) patients, the SMI group 119 (12%) and the MMI group 126 (12.8%). No difference was determined between the groups in respect of

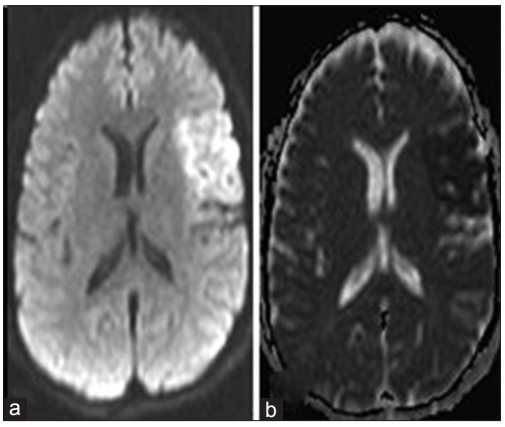

Figure 1: (a and b) Diffusion-weighted imaging and apparent diffusion coefficient map. Single acute infarct in the left middle cerebral artery territory (SI group)

age or gender ($P = 0.580$, $P = 0.157$, respectively). In the SI group, the infarct was in the anterior circulation in 522 (70.3%) patients and in the posterior circulation in 221 (29.7%). In the SMI group, infarcts were determined in the anterior circulation in 57 (47.9%) patients and in the posterior circulation in 62 (52.1%). In the MMI group, infarcts were determined in unilateral anterior and posterior circulation in 56 (44.4%) patients, in bilateral anterior and posterior circulation in 34 (27%) and in bilateral anterior circulation in 36 (28.6%).

Patients were divided into two groups as age below 65 years (35.8%) and older than 65 years (64.2%). The risk factors most determined were HT (65.9%), DM (39.5%) and HL (36.1%) in all patients. No significant difference was determined between the groups in the presence of CAD, DM, and HL. In the MMIs', HT was found significantly higher in age older than 65 years group and malignancy was determined significantly frequent in age below 65 years group ($P = 0.022$, $P = 0.002$, respectively). Risk factors of stroke patients are summarized in Table 1.

The NIHSS score on first application in age below 65 years patients were 4.7 ± 3.4 in the SI group, 5.9 ± 4.8 in the SMI group and 6.0 ± 3.9 in the MMI group. No difference was determined between the groups ($P = 0.809$, ANOVA-Tukey). In older than 65 years patients, NIHSS score was 5.4 ± 3.8 in the SI group, 7.3 ± 5.2 in the SMI group, and 6.4 ± 4.9 in the MMI group. In SMI group, NIHSS score significantly higher than SI group ($P = 0.038$, ANOVA-Tukey). The hematological and biochemical test results of the patients were found to be similar in all the groups ($P > 0.05$, ANOVA-Tukey).

The cardiac evaluation was normal in 682 (69%) patients. The most common cardiac reason was determined as AF in 159 (16.1%) patients. Only 53 (5.4%) patients had a history of AF. In the other 106 patients, the diagnosis of AF was made after stroke. Other cardiac reasons were akinetic left ventricular segment in 32 patients, left atrial thrombus in 9, hypokinetic left ventricular segment in 57, mitral stenosis without AF in 3, dilated cardiomyopathy in 1, and more than one cardiac pathology in 45 patients. AF was determined in 16.4% of the SI group, in 13.4% of the SMI group, and in 16.7% of the MMI group. No statistically significant difference was determined between the groups in respect of cardiac pathologies including AF ($P > 0.05$).

The distribution of etiologies of the patients according to the TOAST classification is shown in Table 2. The most common etiologies were determined to be LAA (SI group 41.5%, SMI group 48.7%, MMI group 40.5%) and CE (SI group 21.7%, SMI group 24.4%, MMI group 25.4%). LAA and CE were

Table 1: Risk factors of stroke patients

	65 ages >				65 ages ≤			
	SI, *n* (%)	SMI, *n* (%)	MMI, *n* (%)	*P**	SI, *n* (%)	SMI, *n* (%)	MMI, *n* (%)	*P**
HT	152 (57.8)	26 (61.9)	26 (53.1)	0.692	328 (68.3)	55 (71.4)	64 (83.1)	0.022
DM	108 (41.1)	18 (42.9)	16 (32.7)	0.505	176 (36.7)	36 (46.8)	36 (46.8)	0.08
HL	112 (42.6)	17 (40.5)	19 (38.8)	0.869	159 (33.1)	25 (32.5)	25 (32.5)	0.989
Coronary arter disease	46 (17.5)	11 (26.2)	11 (22.4)	0.341	106 (22.1)	19 (24.7)	22 (28.6)	0.432
Malignancy	14 (5.3)	1 (2.4)	10 (20.4)	0.002	22 (4.6)	5 (6.5)	6 (7.8)	0.462
CRD	11 (4.2)	0	4 (8.2)	0.077	7 (1.5)	2 (2.6)	5 (6.5)	0.055
Stroke history	63 (24)	16 (38.1)	13 (26.5)	0.152	119 (24.8)	17 (22.1)	18 (23.4)	0.858

*The χ^2 test was used for noncontinuous variables. $P<0.05$ was considered as significant. *n* = Number of patients, SI = Single acute infarct in a single vascular territory, SMI = Multiple acute infarcts in a single vascular territory, MMI = Multiple acute infarcts in multiple vascular territories, HT = Hypertension, DM = Diabetes mellitus, HL = Hyperlipidemia, CRD = Chronic renal disease

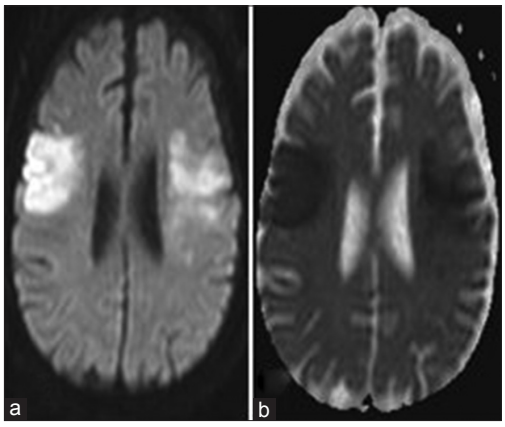

Figure 2: (a and b) Diffusion-weighted imaging and apparent diffusion coefficient map. Multiple acute infarcts in the left middle cerebral artery territory (SMI group)

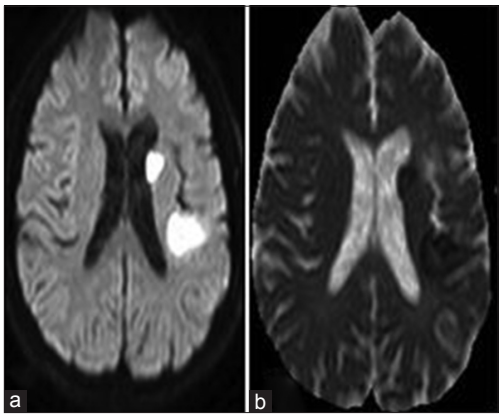

Figure 3: (a and b) Diffusion-weighted imaging and apparent diffusion coefficient map. Multiple acute infarcts in bilateral anterior circulation (MMI group)

determined at similar frequencies in the groups (P = 0.300, P = 0.566, respectively). SVO was determined more in the SI group (SI group 21%, SMI group 6.8%, MMI group 12.7%) (P = 0.0001). Stroke of other determined etiology was determined more in the MMI group (SI group 2%, SMI group 1.7%, MMI group 5.6%) but did not reach statistical significance (P = 0.05). The rates of stroke of undetermined etiology were similar in all the groups (SI group 13.9%, SMI group 18.5%, and MMI group 15.9%) (P = 0.383). In patients with multiple acute infarcts in bilateral anterior and posterior circulation, CE was determined at a higher rate (38.2%) and in patients with multiple acute infarcts in bilateral anterior circulation or unilateral anterior and posterior circulation, the most common cause was LAA (38.9%, 48.2%, respectively).

Patients in the MMI group comprised 10 (6.5%) of the 153 patients who were taken DWI within the first 6 h after stroke onset, 70 (8.5%) of the 825 in the first 24 h, 92 (10.4%) of the 884 in the first 48 h, 114 (12.1%) of the 939 in the first 72 h, and 12.8% of all the patients in the first 7 days.

Discussion

The results of this study showed that SMI was determined in 12% of patients and MMI in 12.8%. The previous studies have shown the frequency of multiple acute infarcts ranging from 4.6% to 37.1%.[2-20] The probable reasons for the results to be sodifferent are differences in the definition of multiple acute infarcts, the imaging methods used in the diagnosis and the time elapsed from stroke onset to imaging. In the current study, patients with multiple acute infarcts in multiple vascular territories were defined as the MMI group and those with multiple acute infarcts in a singular vascular territory as the SMI group.

In early studies, CT or conventional MR imaging were used in the diagnosis of ischemic stroke. Those studies determined multiple acute infarcts of posterior circulation ischemia in 11% and anterior circulation ischemia in 5%.[21,22] The disadvantages of CT are that in the early stage of infarct, the appearance may be normal and small punctate infarcts, especially in the posterior circulation may be missed. In addition, as clinically silent infarcts are not uncommon, it may not be possible to determine whether or not all the multiple infarcts determined with CT, and conventional MR imaging are acute. DWI is superior to CT and conventional MR imaging in detecting acute infarcts.[23] Acute infarcts are characterized by hyperintense signals on DWI and hypointense signals on ADC map.[24] ADC map may allow the differentiation of acute from subacute and chronic ischemic lesions. In the current study, DWI and ADC map were used to confirm multiple infarcts as truly acute.

Table 2: Trial of Org 10172 in acute stroke treatment classification

	Total	SI, *n* (%)	SMI, *n* (%)	MMI, *n* (%)	*P**
LAA	417 (42.2)	308 (41.5)	58 (48.7)	51 (40.5)	0.300
CE	222 (22.5)	161 (21.7)	29 (24.4)	32 (25.4)	0.566
SVO	180 (18.2)	156 (21.0)	8 (6.8)	16 (12.7)	0.0001
Stroke of other determined etiology	24 (2.4)	15 (2.0)	2 (1.7)	7 (5.6)	0.05
Stroke of undetermined etiology	145 (14.7)	103 (13.9)	22 (18.5)	20 (15.9)	0.383

*The χ^2 test was used for noncontinuous variables. P<0.05 was considered as statistically significant. SI = Single acute infarct in a single vascular territory, SMI = Multiple acute infarcts in a single vascular territory, MMI = Multiple acute infarcts in multiple vascular territories, LAA = Large artery atherosclerosis, CE = Cardioembolism, SVO = Small vessel occlusion

Another possible reason for the difference in study results is the difference in time from onset of ischemic stroke to imaging. In the previous studies made with DWI, the rates of multiple acute infarcts have been reported to be 16.8%–25.6% at 24 h,[3,9,13] 9.7% at 36 h,[2] 9.8%–33% at 48 h,[5,6] 4.6%–24.4% at 72 h,[7,8,16] 28.9%–37.1% at 4 days,[19,20] 13.5% at 5 days,[11] 9.7%–16% at 7 days,[4,17,18] and 13.4% at 15 days.[14] That low rate was determined in the study by Saito *et al*. could be due to the inclusion of patients only with infarct in bilateral anterior circulation.[7] In three studies where the definition of multiple acute infarcts was made in the same way as in the our study, rates have been reported as 17% at 24 h,[13] 9.7% at 36 h,[2] and 9.8% at 48 h.[6] Ueno *et al*. also used the same definition as in the our study and similarly reported that within 7 days 13% of patients were in the SMI group and 11% in the MMI group.[10] It has been reported that at the end of the 1st week, new DWI lesions can be determined in ischemic stroke patients at rates of up to 38%.[13,25,26] Therefore, when imaging is delayed there is the possibility that the multiple infarcts determined have not developed simultaneously but on consecutive days. In our study, as the time to taking of DWI extended, a greater number of patients were determined with multiple acute infarcts.

It is important whether the etiology of multiple acute infarcts is different or not from that of a single infarct. Because the most important parameter in determining the treatment to be applied as secondary prophylaxis for stroke patients is the etiology of the stroke. Previous studies were reported that multiple acute infarcts often develop as a result of emboli and emboli may be multiple or a fragmented single embolism in the form of an embolic shower.[15] In a study, a cardiac source was determined in 49% of patients with multiple acute infarcts[2] while Cho *et al*. determined an isolated cardioembolic mechanism in only 29.9%.[6] Another study reported a relationship between multiple acute infarcts and mobile aortic plaque.[10] However, some studies have reported SVO to be the main mechanism of multiple acute infarcts.[11,27,28] However, these results could be due to these studies not having conducted sufficient cardiac examination (e.g., TTE) or that only lacunar infarcts were included in the studies.[11,27,28] Hematological diseases and malignancies have also been reported as other causes of multiple acute infarcts.[19,29] In our study, malignancy was more frequent in the MMI group in age below 65.

The most common etiologies were determined to be LAA and CE in all groups. Moreover, we did not determined the difference between the groups in respect of the frequency of LAA and CE. As in other studies, CE was determined more often in the etiology of patients with MMI in bilateral anterior and posterior circulation.[5,19] The most common cause in patients with MMI in bilateral anterior circulation or unilateral anterior and posterior circulation was LAA. In some studies, LAA[19] has been determined more in patients with multiple acute infarcts in bilateral anterior circulation and in other studies, CE.[3]

SMI was determined in 12% of the current study patients. In previous studies, the SMI rate has been reported between 7% and 40% at 24 or 48 h.[3,5,13] Koennecke *et al*. determined SMI in 32 of 62 ischemic stroke patients when DWI was taken within the first 10 days.[30]

No difference has been found between multiple acute infarcts patients and single infarct patients in respect of gender, HL, HT, smoking, and DM.[2,8,9] In some studies, a relationship has been found between the development of multiple acute infarcts and advanced age,[10,11] previous ischemic stroke,[11] CAD,[10] and high NIHSS on admission.[10] Although some studies have found no relationship between AF and the development of multiple acute infarcts,[9,11] others have found AF more frequently in multiple acute infarcts patients.[8] Similarly, no difference has been found between SMI patients and SI patients in respect of HT, DM, smoking, hypercholesterolemia, gender, and age.[30] In the current study, the most commonly determined risk factors were HT and DM, although the rates were not different between the groups. In the MMI group, malignancy and CRD were more often determined. The NIHSS on presentation and the laboratory values examined were not found to be different in any of the groups.

As the current study was retrospective, there were some limitations. The most significant limitation was that a complete cardiac evaluation was not made of all patients. ECG and TTE were evaluated to all patients but not TEE and Holter ECG. Therefore, embolic reasons such as paroxysmal AF may not have been determined, and embolism from the heart may have been underestimated. Another limitation is that as angiography was not performed to all patients, variations may have been overlooked. In our study, we emphasized the importance of etiological factors in the distribution of acute ischemic lesions. However, in addition to lesions distrubition, evaluating the ischemia in the cortical regions and observing the hemorrhagic transformation may be important in the etiology of the disease.

Conclusion

Multiple acute infarcts on DWI are not an uncommon finding. Moreover, there were no differences between patients with single acute infarct and those with multiple acute infarcts in respect of stroke etiology and risk factor.

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Conflicts of interest

There are no conflicts of interest.

References

1. Kernan WN, Ovbiagele B, Black HR, Bravata DM, Chimowitz MI, Ezekowitz MD, *et al.* Guidelines for the prevention of stroke in patients with stroke and transient ischemic attack: A guideline for healthcare professionals from the american heart association/American stroke association. Stroke 2014;45:2160-236.
2. Depuydt S, Sarov M, Vandendries C, Guedj T, Cauquil C, Assayag P, *et al.* Significance of acute multiple infarcts in multiple cerebral circulations on initial diffusion weighted imaging in stroke patients. J Neurol Sci 2014;337:151-5.
3. Kang DW, Chalela JA, Ezzeddine MA, Warach S. Association of ischemic lesion patterns on early diffusion-weighted imaging with TOAST stroke subtypes. Arch Neurol 2003;60:1730-4.
4. Seifert T, Enzinger C, Storch MK, Pichler G, Niederkorn K, Fazekas F. Acute small subcortical infarctions on diffusion weighted MRI: Clinical presentation and aetiology. J Neurol Neurosurg Pcychiatry 2005;76:1520-4.
5. Wessels T, Wessels C, Ellsiepen A, Reuter I, Trittmacher S, Stolz E, *et al.* Contribution of diffusion-weighted imaging in determination of stroke etiology. AJNR Am J Neuroradiol 2006;27:35-9.
6. Cho AH, Kim JS, Jeon SB, Kwon SU, Lee DH, Kang DW, *et al.* Mechanism of multiple infarcts in multiple cerebral circulations on diffusion-weighted imaging. J Neurol 2007;254:924-30.
7. Saito K, Moriwaki H, Oe H, Miyashita K, Nagatsuka K, Ueno S, *et al.* Mechanisms of bihemispheric brain infarctions in the anterior circulation on diffusion-weighted images. AJNR Am J Neuroradiol 2005;26:809-14.
8. Takahashi K, Kobayashi S, Matui R, Yamaguchi S, Yamashita K. The differences of clinical parameters between small multiple ischemic lesions and single lesion detected by diffusion-weighted MRI. Acta Neurol Scand 2002;106:24-9.
9. Wen HM, Lam WW, Rainer T, Fan YH, Leung TW, Chan YL, *et al.* Multiple acute cerebral infarcts on diffusion-weighted imaging and risk of recurrent stroke. Neurology 2004;63:1317-9.
10. Ueno Y, Kimura K, Iguchi Y, Shibazaki K, Inoue T, Hattori N, *et al.* Mobile aortic plaques are a cause of multiple brain infarcts seen on diffusion-weighted imaging. Stroke 2007;38:2470-6.
11. Lee JH, Kim YJ, Moon Y, Cho HJ, Kim HY. Acute simultaneous multiple lacunar infarcts: A severe disease entity in small artery disease. Eur Neurol 2012;67:303-11.
12. Adams HP Jr., Bendixen BH, Kappelle LJ, Biller J, Love BB, Gordon DL, *et al.* Classification of subtype of acute ischemic stroke. Definitions for use in a multicenter clinical trial. TOAST. Trial of org 10172 in acute stroke treatment. Stroke 1993;24:35-41.
13. Braemswig TB, Usnich T, Albach FN, Brunecker P, Grittner U, Scheitz JF, *et al.* Early new diffusion-weighted imaging lesions appear more often in stroke patients with a multiple territory lesion pattern. Stroke 2013;44:2200-4.
14. Altieri M, Metz RJ, Müller C, Maeder P, Meuli R, Bogousslavsky J, *et al.* Multiple brain infarcts: Clinical and neuroimaging patterns using diffusion-weighted magnetic resonance. Eur Neurol 1999;42:76-82.
15. Baird AE, Lövblad KO, Schlaug G, Edelman RR, Warach S. Multiple acute stroke syndrome: Marker of embolic disease? Neurology 2000;54:674-8.
16. Ay H, Oliveira-Filho J, Buonanno FS, Ezzeddine M, Schaefer PW, Rordorf G, *et al.* Diffusion-weighted imaging identifies a subset of lacunar infarction associated with embolic source. Stroke 1999;30:2644-50.
17. Caso V, Budak K, Georgiadis D, Schuknecht B, Baumgartner RW. Clinical significance of detection of multiple acute brain infarcts on diffusion weighted magnetic resonance images. J Neurol Neurosurg Pcychiatry 2005;76:514-8.
18. Chung JW, Park SH, Kim N, Kim WJ, Park JH, Ko Y, *et al.* Trial of ORG

10172 in acute stroke treatment (TOAST) classification and vascular territory of ischemic stroke lesions diagnosed by diffusion-weighted imaging. J Am Heart Assoc 2014;3:e001119.
19. Roh JK, Kang DW, Lee SH, Yoon BW, Chang KH. Significance of acute multiple brain infarction on diffusion-weighted imaging. Stroke 2000;31:688-94.
20. Zhang C, Zhao X, Wang C, Liu L, Ding Y, Akbary F, *et al.* Prediction factors of recurrent ischemic events in one year after minor stroke. PLoS One 2015;10:e0120105.
21. Bernasconi A, Bogouslavssky J, Bassetti C, Regli F. Multiple acute infarcts in the posterior circulation. J Neurol Neurosurg Psychiatry 1996;60:289-96.
22. Bogousslavsky J, Bernasconi A, Kumral E. Acute multiple infarction involving the anterior circulation. Arch Neurol 1996;53:50-7.
23. Schellinger PD, Bryan RN, Caplan LR, Detre JA, Edelman RR, Jaigobin C, *et al*. Evidence-based guideline: The role diffusion and perfusion MRI for the diagnosis of acute ischemic stroke. Report of the therapeutics and technology assessment subcommittee of the American Academy of Neurology. Neurology 2010;75:177-85.
24. Bonati LH, Lyrer PA, Wetzel SG, Steck AJ, Engelter ST. Diffusion weighted imaging, apparent diffusion coefficient maps and stroke etiology. J Neurol 2005;252:1387-93.
25. Asdaghi N, Hameed B, Saini M, Jeerakathil T, Emery D, Butcher K, *et al.* Acute perfusion and diffusion abnormalities predict early new MRI lesions 1 week after minor stroke and transient ischemic attack. Stroke 2011;42:2191-5.
26. Nolte CH, Albach FN, Heuschmann PU, Brunecker P, Villringer K, Endres M, *et al.* Silent new DWI lesions within the first week after stroke. Cerebrovasc Dis 2012;33:248-54.
27. Chowdhury D, Wardlaw JM, Dennis MS. Are multiple acute small subcortical infarctions caused by embolic mechanisms? J Neurol Neurosurg Psychiatry 2004;75:1416-20.
28. Wolf ME, Sauer T, Kern R, Szabo K, Hennerici MG. Multiple subcortical acute ischemic lesions reflect small vessel disease rather than cardiogenic embolism. J Neurol 2012;259:1951-7.
29. Fagniez O, Tertian G, Dreyfus M, Ducreux D, Adams D, Denier C, *et al.* Hematological disorders related cerebral infarctions are mostly multifocal. J Neurol Sci 2011;304:87-92.
30. Koennecke HC, Bernarding J, Braun J, Faulstich A, Hofmeister C, Nohr R, *et al.* Scattered brain infarct pattern on diffusion-weighted magnetic resonance imaging in patients with acute ischemic stroke. Cerebrovasc Dis 2001;11:157-63.