Clinical Features and Functional Outcome of Stroke After Transient Ischemic Attack

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Background: Transient ischemic attacks (TIAs) greatly increase the risk of stroke, but few reports have examined subsequent stroke in patients with history of TIA. *Methods:* This retrospective, hospital-based study included 506 consecutive patients with acute ischemic stroke who were admitted to our hospital. The clinical features and prognosis were compared between patients with and without TIA. Multiple logistic regression analysis was also performed to identify predictors for poor outcome. *Results:* Of 506 patients, 114 (22.5%) had a history of TIA. Compared to patients without previous TIAs (non-TIA group), patients with previous TIAs (TIA group) were significantly more likely to have hypertension (76.3% vs 64.3%; $P = .016$), dyslipidemia (57.0% vs 41.1%; $P = .003$), chronic kidney disease (28.1% *v* 15.1%; $P = .001$), intracranial major artery stenosis (51.8% vs 36.2%; $P = .018$), and large artery atherothrombosis (43.9% vs 28.3%; $P = .002$). There was no difference in the previous use of antithrombotic medications between the groups (36.0% vs 35.2%; $P = .881$). Although stroke severity on admission was similar, poor functional outcome (modified Rankin Scale score ≥4) was significantly more frequent in the TIA group, and history of TIA was an independent determinant of unfavorable outcome on multiple logistic regression analysis (odds ratio 1.46; 95% confidence interval 1.02–2.10; $P = .041$). *Conclusions:* Atherothrombotic stroke with concomitant vascular risk factors were more frequent in the stroke patients with than without previous TIA. Antithrombotic therapy was conducted only in one-third of the patients even after TIA. The stroke patients with history of TIA were at great risk of disabling stroke. **Key Words:** Acute stroke—clinical features—functional outcome—transient ischemic attack.

Transient ischemic attack (TIA) is a widely recognized warning sign for subsequent stroke. However, because the symptoms of this "warning event" disappear in a short time, even without any treatment, they tend to be disregarded or ignored by both patients and their families. For the same reason, even general physicians sometimes attach low priority to such symptoms. However, many clinical studies have shown that patients are at great risk immediately after TIA, and the short-term risk of stroke has been a focus of attention.[1-9] There has been much research showing the need for urgent assessment and treatment of TIA,[10,11] but detailed reports about the status of acute ischemic stroke in patients with a history of TIA are limited. Clarification of the effect of TIA on the subsequent course of recurrent stroke may be extremely useful information in considering strategies for preventing recurrent stroke after TIA. Therefore, a hospital-based study to investigate clinical features

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and functional outcomes of acute ischemic stroke patients with a history of TIA compared to those without a history of TIA was conducted.

Materials and Methods

Subjects

A retrospective, hospital-based study was conducted involving 515 consecutive acute ischemic stroke patients hospitalized in the Department of Neurology at Tokyo Women's Medical University Hospital between April 2005 and March 2010. Eligible patients were those within 1 week of the onset of their first symptomatic ischemic stroke and who were independent in activities of daily living with a modified Rankin Scale (mRS) score ≤2 before the stroke. After excluding 9 patients because they were lost to follow-up or moved out of the region, 506 patients were included in the analysis. These stroke patients were divided into 2 groups: 1 with history of TIA (TIA group) and 1 without such history (non-TIA group), and their respective clinical features and outcomes were compared.

Protocol

The ethics committee of our institution approved the protocol of this study. Data were collected from a computerized observational database, imaging data, and medical records of other hospitals or private practitioners. Our clinic keeps a prospective registry of all consecutive patients. We used a standardized case report form and abstracted a number of demographic and clinical variables including date of the event, medical history, risk factors for stroke, previous medications, previous TIA, physiologic, examination findings and neurologic symptoms. We also documented the results of all diagnostic tests and details of treatment performed during hospitalization. The person imputing data was blinded to the purpose of this study.

At the time of hospitalization, demographic characteristics, medication history, risk factors for stroke, and history of TIA were thoroughly investigated, and a blood sample, chest radiograph, electrocardiogram (ECG), and computed tomographic (CT) scan of the head were obtained. A magnetic resonance imaging (MRI) scan or magnetic resonance angiographic (MRA) scan of the head was performed in 501 patients, after excluding those with cardiac pacemakers or other contraindications. These were all performed within 24 hours of hospital admission. The information was also collected from private practitioners and other hospitals by fax or mail. All strokes were diagnosed by stroke neurologists based on neurologic observations and MRI or CT findings. The vascular territories of ischemia were classified as (1) left anterior circulation, (2) right anterior circulation, (3) posterior circulation, or (4) multiple. Assessments were made for severity of the event according to the National Institute of Health Stroke Scale (NIHSS); NIHSS scores range from 0 to 42, with higher values reflecting more severe neurologic deficits.

Ischemic stroke was defined as an episode of focal neurologic deficits with acute onset lasting >24 hours (or lasting <24 hours with imaging evidence of stroke corresponding with current symptoms). TIA was defined as an acute loss of cerebral or ocular function lasting <24 hours and without corresponding imaging evidence of an ischemic lesion. In accordance with the recommendations of international guidelines,[12] all information obtained from the patients, relatives, caregivers, and medical records of our hospital, other hospitals, or private practitioners were evaluated, and a final diagnosis of TIA was based on the consensus agreement of 2 or more board-certified stroke neurologists. Patients with disagreements of the diagnosis of TIA were excluded from this study. Patients who had not undergone brain imaging during or shortly after TIA were also excluded.

Diagnostic tests during hospitalization included carotid artery ultrasound, transthoracic cardiac ultrasound, and Holter ECG in all patients, plus transcranial Doppler ultrasound, transesophageal echocardiography, 3-dimensional CT angiography (CTA), digital subtraction angiography, and cerebral blood flow single-photon emission computed tomography in some patients when clinically indicated. In patients in whom findings suggesting a right-to-left shunt were confirmed, the presence or absence of venous thrombi was checked with leg vein ultrasound or full body contrast CT or magnetic resonance venography. All cardiac evaluations were conducted by trained cardiologists. The treatment regimen for each patient was determined in accordance with the international consensus by a neurologist with experience treating neurovascular disease.

Stroke-related disability/handicap was assessed by an attending doctor of our hospital with the mRS at the 3-month follow-up. When the patients could not attend the follow-up appointment, we contacted their family members or the staff of rehabilitation center or nursing home by phone. Patients who had died by 3 months were scored as mRS score 6. Poor functional outcome was defined as an mRS score ≥4.

Baseline Risk Factors

Body mass index was measured as kg/m^2. Hypertensive patients were defined as those who were receiving antihypertensive treatment at the time of the event, or those with continuing high values of systolic blood pressure (SBP) ≥140 mm Hg or diastolic blood pressure (DBP) ≥90 mm Hg after >1 week had passed since the event. Patients with diabetes mellitus were defined as those who had previously been diagnosed with type 1 or 2 diabetes, or those with fasting blood glucose ≥126 mg/dL

or blood glucose ≥200 mg/dL on 2 random measurements. Patients with dyslipidemia were defined as those who had been receiving lipid-lowering treatment at the time of the event, or those with serum low-density lipoprotein cholesterol ≥140 mg/dL, high-density lipoprotein cholesterol ≤40 mg/dL, or serum triglycerides ≥150 mg/dL. The estimated glomerular filtration rate (eGFR) was calculated from the modification of diet in renal disease formula by the Japanese coefficient; chronic kidney disease (CKD) was defined as an eGFR <60 mL/min/1.73 m^2. Smoking status was determined based on whether or not the patient was a current smoker. Intracranial arterial stenosis ≥50% on MRA, CTA, or angiograms was considered significant. Carotid artery ultrasounds were read by appropriately trained neurologists, and stenosis ≥50% was defined as significant extracranial arterial stenosis. Patients with either significant intra- or extracranial artery stenosis were considered to have major artery lesions. The history of ischemic heart disease (IHD; myocardial infarction or angina pectoris) and peripheral arterial disease (PAD) was recorded, and any kind of medical condition in the past was taken to be a previous condition. Atrial fibrillation (AF) was judged based on 2 or more ECGs taken before or during hospitalization. All patients were invariably under continuous ECG monitoring during the acute phase.

Stroke Subtypes

Subtypes classified by etiology were large artery atherosclerosis (LAA), cardioembolism (CE), small-vessel occlusion (SV), other cause (OC), or undetermined cause (UND), in conformity with the Trial of Org 10172 in Acute Stroke Treatment (TOAST) criteria.[13] Stroke subtype was assigned to each patient by pairs of investigators during hospitalization. In cases of discrepancy, the patient records were reviewed by a few senior investigators, and the final categorization was based on their consensus agreement.

Statistical Analysis

Analyses were performed with SPSS software (v 11.0; SPSS Inc., Chicago, IL). Statistical significance for intergroup differences was assessed by the Chi-square test for categorical variables and the Student t or Mann–Whitney U tests were used for continuous variables. To identify predictors for poor outcome, we performed multiple logistic regression analysis based on a forward stepwise method including all variables with P values <.25 in univariate analysis as follows: history of TIA, SBP ≥140 mm Hg, DBP ≥90 mm Hg, major artery stenosis, history of PAD, AF, and NIHSS score at admission. Because of their clinical relevance and potential importance, age ≥75 years, other vascular risk factors (diabetes mellitus, dyslipidemia, CKD, and smoking), history of IHD, previous antithrombotic therapy, and thrombolytic therapy were retained in the final regression model. Stroke subtypes were excluded from the model because LAA and CE have multicolinearities with major artery stenosis and AF, respectively. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated. In all analyses, $P < .05$ was considered significant (2-sided test).

Results

Clinical Features

The subjects in this study were 506 acute stroke patients (mean age 68.5 years; 63.6% males). All patients were of Asian descent. Of 506 patients, 114 (22.5%) had a history of TIA. Table 1 shows a comparison of patient characteristics between patients with history of TIA and those without history of TIA. There were no differences between the groups in age, sex, or length of hospitalization. In a comparison of vascular risk factors, the TIA group had significantly higher percentages for hypertension (76.3% vs 64.3%; $P = .016$), dyslipidemia (57.0% vs 41.1%; $P = .003$), and CKD (28.1% vs 15.1%; $P = .001$). There were no differences with regard to diabetes mellitus or current smoking. Patients in the TIA group had a greater number of vascular risk factors (hypertension, diabetes mellitus, dyslipidemia, CKD, and current smoking) than those in the non-TIA group (mean 2.2 vs 1.7; $P < .001$). The TIA group also had significantly more patients with intracranial major artery stenosis (51.8% vs 36.2%; $P = .003$) and a history of PAD (8.8% vs 3.1%; $P = .009$). The prevalence of AF was nearly equal (30.3% vs 27.3%; $P = .476$).

With regard to stroke subtypes, the percentage of LAA was found to be significantly higher in the TIA group than in the non-TIA group (43.9% vs 28.3%; $P = .002$), while there were no differences in the percentages of CE or SV between the groups. Among patients in whom the subtype was OC, 1 of the patients with antiphospholipid syndrome had a history of TIA.

There were no differences between the 2 groups in the distribution of vascular territories of ischemia, in the percentage of patients who had been receiving antithrombotic therapy before the stroke (36.0% vs 35.2%; $P = .881$), or in the median NIHSS score at the time of hospitalization (8 vs 8; $P = .321$).

Functional Outcome

Figure 1 and Table 2 show the patients' status 3 months after stroke onset. Of 506 patients, 153 (30.2%) had a poor functional outcome and 10 died. In the TIA group, 44 of 114 patients (38.6%) had a poor outcome, significantly higher than the 109 of 392 patients (27.8%) in the non-TIA group ($P = .027$). An analysis by subtype showed that 50 of 161 patients (31.1%) with LAA, 29 of 161 (18.0%) with CE, and 19 of 98 (19.4%) with SV had history of TIA, and with all subtypes, the percentage of patients with a poor prognosis was higher in the TIA group than

Table 1. *Clinical characteristics of patients with and without a history of transient ischemic attack*

	All	TIA group	Non-TIA group	*P* value (TIA *v* non-TIA)
No. of patients	506	114	392	
Age, y, mean (SD)	68.5 (14.3)	69.6 (12.2)	68.2 (14.9)	.368
Male	322 (63.6%)	78 (68.4%)	244 (62.2%)	.228
Length of hospital stay, days, mean (SD)	28.5 (19.2)	29.6 (17.6)	28.2 (19.7)	.485
Body mass index, kg/m^2, mean (SD)	23.3 (3.5)	23.6 (3.6)	23.2 (3.5)	.350
Vascular risk factors				
Hypertension	339 (67.0%)	87 (76.3%)	252 (64.3%)	.016
Diabetes mellitus	193 (38.1%)	52 (45.6%)	141 (36.0%)	.062
Dyslipidemia	226 (44.7%)	65 (57.0%)	161 (41.1%)	.003
Chronic kidney disease	91 (18.0%)	32 (28.1%)	59 (15.1%)	.001
Current smoking	119 (23.5%)	32 (28.1%)	87 (22.2%)	.193
No. of vascular risk factors, mean (SD)	1.8 (1.1)	2.2 (1.1)	1.7 (1.1)	<.001
SBP, mm Hg, mean (SD)	147.3 (26.4)	152.4 (26.5)	145.8 (26.3)	.019
DBP, mm Hg, mean (SD)	82.3 (15.2)	84.5 (15.6)	81.7 (15.1)	.086
Major artery stenosis	201 (39.7%)	59 (51.8%)	142 (36.2%)	.003
Intracranial	134 (26.5%)	40 (35.1%)	94 (24.0%)	.018
Extracranial	82 (16.2%)	23 (20.2%)	59 (15.1%)	.191
History of ischemic heart disease	101 (20.0%)	27 (23.7%)	74 (18.9%)	.258
History of peripheral artery disease	22 (4.3%)	10 (8.8%)	12 (3.1%)	.009
Atrial fibrillation	142 (28.1%)	35 (30.7%)	107 (27.3%)	.476
Stroke subtype				
Large-artery atherosclerosis	161 (31.8%)	50 (43.9%)	111 (28.3%)	.002
Cardioembolism	161 (31.8%)	29 (25.4%)	132 (33.7%)	.097
Small-vessel occlusion	98 (19.4%)	19 (16.7%)	79 (20.2%)	.407
Other	25 (4.9%)	1 (0.9%)	24 (6.1%)	.023
Undetermined	61 (12.1%)	15 (13.2%)	46 (11.7%)	.681
Vascular territory of ischemia				
Left anterior	174 (%)	42 (36.8%)	132 (33.7%)	.531
Right anterior	170 (%)	41 (36.0%)	129 (32.9%)	.543
Posterior	150 (%)	29 (25.4%)	121 (30.9%)	.264
Multiple lesions	12 (%)	2 (1.8%)	10 (2.6%)	.623
Previous antithrombotic therapy	179 (35.4%)	41 (36.0%)	138 (35.2%)	.881
Antiplatelet therapy	144 (28.5%)	37 (32.5%)	107 (27.3%)	.283
Anticoagulant therapy	46 (9.1%)	8 (7.0%)	38 (9.7%)	.382
NIHSS, median (IQR)	8 (5-12)	8 (6-12)	8 (5-12)	.321

Abbreviations: DBP, diastolic blood pressure; IQR, interquartile range; NIHSS, National Institutes of Health Stroke Scale; SBP, systolic blood pressure; SD, standard deviation; TIA, transient ischemic attack.

Unless otherwise indicated, figures expressed as n (%).

in the non-TIA group, although the difference was not significant. The results of multivariate analysis showed that history of TIA was an independent predictor of poor outcome at 3 months (OR 1.46; 95% CI 1.02-2.10; $P = .041$; Table 3). Other significant factors were major artery stenosis (OR 1.63; 95% CI 1.15-2.33; $P = .007$), AF (OR 1.52; 95% CI 1.04-2.23; $P = 0.03$), and NIHSS score on admission (OR 1.72; 95% CI 1.56-1.93; $P < .001$).

Discussion

In the present study, atherothrombotic stroke with concomitant vascular risk factors was more frequent in stroke patients with a history of TIA than in those without a history of TIA. In addition, although the NIHSS score at the time of hospitalization was nearly equal in the 2 groups, there were significantly more patients with poor outcome in the TIA group. On multivariate analysis, a history of TIA was found to be an independent predictor of poor outcome.

In our hospital-based study, the percentage of stroke patients who had experienced TIA was 22.5% (114/506).

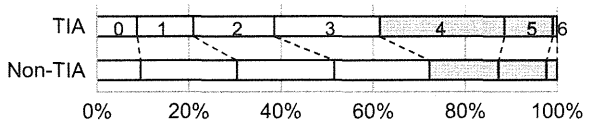

Figure 1. *Distribution of modified Rankin Scale scores 3 months after stroke onset.*

Table 2. *Percentage of poor outcomes at 3 months, overall and by subtype*

	TIA	Non-TIA	*P* value
All (n = 506)			
No. of patients	114	392	
mRS, median (IQR)	3 (2-4)	2 (1-4)	
mRS ≥4	44 (38.6%)	109 (27.8%)	.027
mRS 6	1 (0.9%)	9 (2.3%)	.338
Large artery atherosclerosis (n = 161)			
No. of patients	50	111	
mRS ≥4	24 (48.0%)	39 (35.1%)	.122
Cardioembolism (n = 161)			
No. of patients	29	132	
mRS ≥4	13 (44.8%)	49 (37.1%)	.44
Small-vessel disease (n = 98)			
No. of patients	19	79	
mRS ≥4	2 (10.5%)	3 (3.8%)	.231

Abbreviations: IQR, interquartile range; mRS, modified Rankin Scale.

Unless otherwise indicated, figures expressed as n (%).

Table 3. *Multiple logistic regression analysis for poor outcome*

	OR (95% CI)	*P* value
History of TIA	1.46 (1.02-2.10)	.041
Age ≥75 y	1.26 (0.99-1.77)	.18
SBP ≥140 or DBP ≥90 mm Hg	1.20 (0.86-1.68)	.29
Diabetes mellitus	1.01 (0.79-1.49)	.60
Dyslipidemia	0.98 (0.70-1.37)	.92
Chronic kidney disease	0.94 (0.63-1.39)	.76
Current smoking	1.10 (0.75-1.61)	.61
Major artery stenosis	1.63 (1.15-2.33)	.007
History of ischemic heart disease	0.79 (0.50-1.21)	.28
History of peripheral artery disease	1.49 (0.76-2.91)	.24
Atrial fibrillation	1.52 (1.04-2.23)	.03
Prior antithrombotic therapy	1.08 (0.74-1.58)	.66
NIHSS score on admission	1.72 (1.56-1.93)	<.001
Thrombolytic therapy	0.63 (0.16-2.05)	.50

Abbreviations: CI, confidence interval; DBP, diastolic blood pressure; NIHSS, National Institutes of Health Stroke Scale; OR, odds ratio; SBP, systolic blood pressure; TIA, transient ischemic attack.

This percentage was particularly high in LAA patients (31.1%). In previous reports, the prevalence of a previous TIA among patients who presented with stroke has been reported to be wide-ranging. The percentage varies, depending on such factors as how TIA is defined, which stroke subtypes are evaluated, and whether the study is population- or hospital-based.[14,15] In the population-based Northern Manhattan Stroke study, the prevalence of TIAs among those who presented with first ischemic stroke was 8.7%.[16] Studies that have included patients with previous stroke, such as the Harvard Stroke Registry and National Institute of Neurological Disorders and Stroke databank, have reported higher rates of TIAs—as high as 50% among those with atherothrombotic stroke.[17,18] However, because TIA was defined without consideration of the presence or absence of imaging findings of stroke, the percentage may be overestimated when a new definition is used.

The percentages of etiologic subtypes among all stroke patients differ greatly by country and race.[19-22] In our study, LAA and CE accounted for about one-third of patients, which is similar to a past report in Japan.[23] Purroy et al[24] investigated the risk of recurrence after TIA with respect to etiologic subtype and reported that the stroke risk was higher in LAA patients than in other subtypes. We also found that there were many LAA stroke patients after TIA, and obtained new findings that their functional outcome was poorer than that of patients who had not experienced TIA. Differences were not significant in an analysis by subtype, but there tended to be more patients with poor outcomes in all subtypes. However, these findings seem to be quite contrary to the conception of "ischemic tolerance." In a number of animal models, reduced impact of ischemia after an initial ischemic insult—ischemic preconditioning—has been shown.[25] The degree of protection from infarction is supposed to be greater with longer duration and greater distribution or severity of the initial ischemia and dependent on the duration between the initial and subsequent injuries. Several clinical studies also have suggested that ischemic strokes are less severe in patients with previous TIA,[26-29] but each has limitations inherent in observational studies. That is, location, duration, and etiology of previous TIA are not always reliable from clinical history and there is no real measure of "dose" or severity of the ischemia. In addition, TIA often precipitates treatment with prophylactic medications, and these medications may impact outcomes. Considering that the condition of artificial ischemia in animal models is different from that of clinical TIA based on multiple vascular risk factors, it may be hard to entirely reconcile with animal studies.

This study had limitations. First, it was a retrospective study. We conducted an analysis based on a computerized database created during the period of patient hospitalization and postdischarge follow-up. Second, because it was a hospital-based study, the characteristics of the cohort may have differed from those of the general community population. These limitations might affect our findings. This study did not investigate the $ABCD^2$ score, length of TIA, territory of TIA, and the time after TIA until stroke recurrence. With regard to multivariate analysis,

prestroke activities of daily living and infectious complications during hospitalization could be confounding factors for poor functional outcome, but the accurate information of these factors was unavailable retrospectively. As to the prestroke activities of daily living, we investigated whether the activity of the patients' daily living had been independent (mRS ≤2) or not. We should have included these factors in the model for precise analysis. It is generally accepted that diabetes[30-32] and CKD[33,34] are associated with poor functional outcome in ischemic stroke, but these factors were not significantly associated with poor functional outcome in our study. The discrepancy might be related to the small sample size and imperfect multivariate model. We included previously diagnosed patients in defining vascular risk factors, and not a few of them had been treated before stroke. We did not take the condition of previous treatment into account, and it potentially affected the results. The subjects of our study seemed to be younger than those of previous reports that revealed a poor outcome in stroke patients with diabetes[30-32] or CKD[33,34]; therefore, the younger age of our subjects might also affect the results. Although additional studies are needed to examine our findings, our study may provide important and useful information in considering stroke prevention strategies in patients with TIA.

References

1. Kleindorfer D, Panagos P, Pancioli A, et al. Incidence and short-term prognosis of transient ischemic attack in a population-based study. Stroke 2005;36:720-723.
2. Lisabeth LD, Ireland JK, Risser JM, et al. Stroke risk after transient ischemic attack in a population-based setting. Stroke 2004;35:1842-1846.
3. Johnston SC, Gress DR, Browner WS, et al. Short-term prognosis after emergency department diagnosis of TIA. JAMA 2000;284:2901-2906.
4. Eliasziw M, Kennedy J, Hill MD, et al., North American Symptomatic Carotid Endarterectomy Trial Group. Early risk of stroke after a transient ischemic attack in patients with internal carotid artery disease. CMAJ 2004;170: 1105-1109.
5. Coull AJ, Lovett JK, Rothwell PM, on behalf of the Oxford Vascular Study. Population based study of early risk of stroke after transient ischaemic attack or minor stroke: Implications for public education and organisation of services. BMJ 2004;328:326.
6. Hill MD, Yiannakoulias N, Jeerakathil T, et al. The high risk of stroke immediately after transient ischemic attack: A population-based study. Neurology 2004;62:2015-2020.
7. Daffertshofer M, Mielke O, Pullwitt A, et al. Transient ischemic attacks are more than "ministrokes". Stroke 2004;35:2453-2458.
8. Gladstone DJ, Kapral MK, Fang J, et al. Management and outcomes of transient ischemic attacks in Ontario. CMAJ 2004;170:1099-1104.
9. Rothwell PM, Giles MF, Flossmann E, et al. A simple score (ABCD) to identify individuals at high early risk of stroke after transient ischaemic attack. Lancet 2005; 366:29-36.
10. Rothwell PM, Giles MF, Chandratheva A, et al. Effect of urgent treatment of transient ischaemic attack and minor stroke on early recurrent stroke (EXPRESS study): A prospective population-based sequential comparison. Lancet 2007;370:1432-1442.
11. Lavallée PC, Meseguer E, Abboud H, et al. A transient ischaemic attack clinic with round-the-clock access (SOS-TIA): Feasibility and effects. Lancet Neurol 2007; 6:953-960.
12. Pearson TA, Blair SN, Daniels SR, et al. AHA Guidelines for Primary Prevention of Cardiovascular Disease and Stroke: 2002 Update: Consensus Panel Guide to Comprehensive Risk Reduction for Adult Patients Without Coronary or Other Atherosclerotic Vascular Diseases. American Heart Association Science Advisory and Coordinating Committee. Circulation 2002;106:388-391.
13. Adams HP, Bendixen BH, Kappelle LJ, 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.
14. Dennis M, Bamford J, Sandercock P, et al. Prognosis of transient ischemic attacks in the Oxfordshire Community Stroke Project. Stroke 1990;21:848-853.
15. Bogousslavsky J, Van Melle G, Regli F. The Lausanne Stroke Registry: Analysis of 1,000 consecutive patients with first stroke. Stroke 1988;19:1083-1092.
16. Sacco RL. Risk factors for TIA and TIA as a risk factor for stroke. Neurology 2004;62(8 Suppl 6):S7-S11.
17. Mohr JP, Caplan LR, Melski JW, et al. The Harvard Cooperative Stroke Registry: A prospective registry. Neurology 1978;28:754-762.
18. Sacco RL, Ellenberg JH, Mohr JP, et al. Infarcts of undetermined cause: The NINCDS Stroke Data Bank. Ann Neurol 1989;25:382-390.
19. Saposnik G, Caplan LR, Gonzalez LA, et al. Differences in stroke subtypes among natives and caucasians in Boston and Buenos Aires. Stroke 2000;31:2385-2389.
20. Kolominsky-Rabas PL, Weber M, Gefeller O, et al. Epidemiology of ischemic stroke subtypes according to TOAST criteria: Incidence, recurrence, and long-term survival in ischemic stroke subtypes: A population-based study. Stroke 2001;32:2735-2740.
21. Yip PK, Jeng JS, Lee TK, et al. Subtypes of ischemic stroke. A hospital-based stroke registry in Taiwan (SCAN-IV). Stroke 1997;28:2507-2512.
22. Uchino K, Risser JM, Smith MA, et al. Ischemic stroke subtypes among Mexican Americans and non-Hispanic whites: The BASIC Project. Neurology 2004;63:574-576.
23. Kimura K, Kazui S, Minematsu K, et al. Japan Multicenter Stroke Investigator's Collaboration. Analysis of 16,922 patients with acute ischemic stroke and transient ischemic attack in Japan. A hospital-based prospective registration study. Cerebrovasc Dis 2004;18:47-56.
24. Purroy F, Montaner J, Molina CA, et al. Patterns and predictors of early risk of recurrence after transient ischemic attack with respect to etiologic subtypes. Stroke 2007; 38:3225-3229.
25. Kirino T. Ischemic tolerance. J Cereb Blood Flow Metab 2002;22:1283-1296.
26. Yamamoto H, Bogousslavsky J, van Melle G. Different predictors of neurological worsening in different causes of stroke. Arch Neurol 1998;55:481-486.
27. Moncayo J, de Freitas GR, Bogousslavsky J, et al. Do transient ischemic attacks have a neuroprotective effect? Neurology 2000;54:2089-2094.
28. Sitzer M, Foerch C, Neumann-Haefelin T, et al. Transient ischaemic attack preceding anterior circulation infarction

is independently associated with favourable outcome. J Neurol Neurosurg Psychiatry 2004;75:659-660.
29. Castillo J, Moro MA, Blanco M, et al. The release of tumor necrosis factor-alpha is associated with ischemic tolerance in human stroke. Ann Neurol 2003;54:811-819.
30. Jørgensen H, Nakayama H, Raaschou HO, et al. Stroke in patients with diabetes. The Copenhagen Stroke Study. Stroke, 1994 Copenhagen Stroke Study. Stroke 1994; 25:1977-1984.
31. Megherbi SE, Milan C, Minier D, et al, Group EBSoSC. Association between diabetes and stroke subtype on survival and functional outcome 3 months after stroke: Data from the European BIOMED Stroke Project. Stroke 2003;34:688-694.
32. Stöllberger C, Exner I, Finsterer J, et al. Stroke in diabetic and non-diabetic patients: Course and prognostic value of admission serum glucose. Ann Med 2005; 37:357-364.
33. Yahalom G, Schwartz R, Schwammenthal Y, et al. Chronic kidney disease and clinical outcome in patients with acute stroke. Stroke 2009;40:1296-1303.
34. MacWalter RS, Wong SY, Wong KY, et al. Does renal dysfunction predict mortality after acute stroke? A 7-year follow-up study. Stroke 2002;33:1630-1635.