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Outcomes of Mild Stroke and High-Risk Transient Ischemic Attack in Current Clinical Practice

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Keywords
Mild stroke · Stroke · Transient ischemic attack · Outcomes · Progressive stroke

Abstract
Introduction: Early assessment and management of patients with mild stroke and transient ischemic attack (TIA) by specialists were recommended. This study aimed to evaluate the outcomes of these patients and identify the predictive factors of clinical progression, unfavorable outcomes, and recurrent stroke. ***Methods:*** Patients with mild ischemic stroke (NIHSS ≤5) and high-risk TIA were studied. All patients were managed by stroke specialists within 24 h of stroke onset. The outcomes of the patients at 3 months and final follow-up were studied. Predictive factors of clinical progression, unfavorable outcomes, and recurrent stroke were analyzed. ***Results:*** 254 patients were studied. Thirty-eight patients (15%) had clinical progression during admission. Large artery atherosclerosis (OR 2.49, 95% CI: 1.06–5.81), cardioembolism (OR 3.34, 95% CI: 1.26–8.87), and brainstem stroke (OR 2.78, 95% CI: 1.28–6.01) were associated with clinical progression. At the final follow-up, median 22 months, 81 patients (32%) had unfavorable outcomes. Previous disability (OR 1.81, 95% CI: 3.31–100), moderate to severe white matter lesions (OR 2.90, 95% CI: 1.44–5.84), clinical progression (OR 12.5, 95% CI: 5.08–31.25), and recurrent stroke (OR 8.47, 95% CI: 3.21–22.72) were related to unfavorable outcomes. Eleven patients (4%) had recurrent stroke within 3 months and 31 patients (12%) at the final follow-up. Older age (OR 6.68, 95% CI: 2.35–19.02), diabetes mellitus (OR 2.59, 95% CI: 1.07–6.27), and smoking (OR 4.26, 95% CI: 1.52–11.95) were related to recurrent stroke. ***Conclusion:*** Implementation of the up-to-date standard care in clinical practice would bring good clinical outcomes to the patients with mild stroke and high-risk TIA.

Introduction

Mild stroke is common in clinical practice. National Institutes of Health Stroke Scale (NIHSS) scores are used to define the severity of clinical stroke worldwide. Scores of ≤3 or ≤5 are commonly used to identify mild stroke [1–5]. More than half of all ischemic stroke cases have mild severity (NIHSS ≤3) on initial presentation [1]. Previous studies conducted between 1997 and 2003 reported

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the risk of stroke or acute coronary syndrome of 12–20% within the first 3 months after a transient ischemic attack (TIA) or mild stroke [6, 7]. A study, which included patients with minor stroke between 2007 and 2008 from the China National Stroke Registry, reported the rate of recurrent stroke of 9.8% at 3 months [8]. Risk of early recurrent stroke in TIA patients is high, up to 10% in the first 48 h [9, 10]. Over the past decades, there have been advances in stroke prevention strategies. Using high-intensity statin, controlling hypertension with thiazide diuretic, angiotensin-converting enzyme inhibitor or angiotensin II receptor blockers, or using glucose-lowering agents with proven cardiovascular benefit in patients with diabetes is recommended for secondary stroke prevention to reduce the risk of major cardiovascular events, including recurrent stroke [5]. Urgent management in specialized units, including immediate investigations, antithrombotic and other specific treatments, has been shown to significantly reduce risk of recurrent stroke in several large studies [11–13]. In 2016, the TIAregistry.org project, in which most patients were evaluated by a stroke specialist within 24 h, reported lower risk of recurrent stroke: 3.7% at 90 days after symptom onset [13]. Current European Stroke Organization and American Stroke Association guidelines recommend early clinical evaluation in patients with acute stroke and TIA [5, 14], and National Guideline Centre (UK) recommends to immediately refer TIA patients for specialist assessment and investigation, to be seen within 24 h of stroke onset [15].

Several studies focusing on the acute treatment in patients with mild stroke and/or high-risk TIA showed benefit in good functional outcomes and/or reduced risk of recurrent stroke. Intravenous alteplase is recommended to treat eligible patients with mild, but disabling ischemic stroke (NIHSS ≤5), especially within 3 h of symptom onset. In patients with mild noncardioembolic ischemic stroke (NIHSS ≤3) who did not receive intravenous alteplase, treatment with dual antiplatelet (aspirin and clopidogrel) started within 24 h of symptom onset and continued for 21 days is effective in reducing stroke recurrence up to 90 days from symptom onset [2].

Implementation of early assessment and management of patients with mild ischemic stroke and high-risk TIA to routine clinic practice may improve clinical outcomes of these patients. The purpose of the study was to evaluate the outcomes of the patients and identify the predictive factors of clinical progression, unfavorable outcomes, and recurrent stroke.

Methods

Patients with mild ischemic stroke and high-risk TIA who were admitted during July 2018–July 2019 were studied. The inclusion criteria were those with mild stroke (NIHSS ≤5) or high-risk TIA (ABCD2 scores ≥4) within 24 h of stroke onset. Patients enrolled in an antithrombotic trial were excluded. All patients were admitted at the stroke unit and assessed by stroke specialists within 24 h. Electrocardiography was monitored at least 24 h. Neurovascular assessment using magnetic resonance angiography or computed tomography angiography and/or carotid duplex/transcranial Doppler ultrasound was performed in all patients. Intravenous alteplase was given in eligible patients with mild, disabling stroke (NIHSS ≤5). Dual antiplatelet (low-dose aspirin and clopidogrel) was prescribed to patients with mild ischemic stroke (NIHSS ≤3) who were not eligible to receive thrombolytic treatment and to TIA patients with high risk for recurrent stroke (ABCD2 score ≥4) within 24 h of stroke onset, continued for 3 weeks, and then switched to single antiplatelet per the American Stroke Association guideline [5] and the Thai clinical practice guidelines for ischemic stroke [16]. Aspirin 300 mg plus clopidogrel 300 mg were given on day 1, and then, aspirin 75 mg was added to clopidogrel 75 mg on day 2–21 for this regimen. Dual antiplatelet (aspirin 325 mg plus clopidogrel 75 mg) was given for 3 months in those with nondisabling stroke from severe stenosis of major intracranial artery [5, 17]. Others were prescribed with single antiplatelet, mainly aspirin 325 mg, at the acute phase of ischemic stroke in noncardioembolic patients. Single antiplatelet was also given in patients with high risk of bleeding, such as anemic patients or those with history of recent major bleeding. Oral anticoagulant was given in patients with cardioembolic causes, who did not have contraindications for anticoagulant. Electrocardiography was monitored immediately after admission to stroke unit. All treatment regimens were applied within few hours after the admission (mean 2.28 ± 0.73 h). Neuroimaging, at least carotid duplex/transcranial Doppler ultrasound, was performed within 2 days (mean 1.28 ± 0.46 days). Most patients were discharged within a few days if they were clinically stable.

Data, including baseline characteristics, stroke severity, stroke subtypes, clinical course during admission, and clinical outcomes at 3 months and final follow-up, were collected. Progressive stroke was defined by deterioration of clinical stroke during admission or the increase in NIHSS score of at least 1 point compared to admission NIHSS score. Clinical outcomes were evaluated by using Modified Rankin Scale (mRS), with the scores of 0–1 and 2–6 to define favorable and unfavorable outcomes, respectively. Patients who were unable to come to visit at the outpatient clinic would receive telephone calls to evaluate the clinical outcomes by a trained doctor.

The data were presented as a mean or a median for continuous variables and percentage (number) for dichotomous variables. The demographics and vascular risk factors were compared between patients with and without outcomes of interest using Student's *t* test (for the continuous variables) and the χ^2 test (for the proportions). Stepwise multivariate analyses were performed by including the pre-specified factors that were associated with the measured outcome variables in the univariate analysis. The research protocol was approved by the Human Ethic Committee of Thammasat University (project number: MTU-EC-IM-2-257/63).

Table 1. Baseline characteristics of the patients in the study

Baseline characteristics	*n* = 254
Sex, *n* (%)	
Male	171 (67)
Female	83 (33)
Mean age (range)	65 (18–96)
Previous status, *n* (%)	
Independent (mRS0-2)	235 (93)
Walk with instruments/dependent (mRS3-5)	19 (7)
Mean NIHSS on admission (range)	3 (1–5)
Hypertension, *n* (%)	190 (75)
Diabetes mellitus, *n* (%)	89 (35)
Hyperlipidemia, *n* (%)	137 (54)
Coronary artery disease, *n* (%)	29 (11)
Old ischemic stroke, *n* (%)	52 (21)
Atrial fibrillation, *n* (%)	34 (13)
Smoking, *n* (%)	58 (23)
TIA, *n* (%)	24 (9)
Mean ABCD2 score (range)	5.4 (4–6)
Stroke subtypes, *n* (%)	
LAA	41 (18)
SAO	122 (53)
CE	39 (17)
UND	27 (12)
OC	1 (0.4)
Stroke location, *n* (%)	
Cortical lesions	51 (22)
Subcortical white matter lesions, including deep gray	98 (43)
Multiple-territory infarct	23 (10)
Brainstem/cerebellum	58 (25)
White matter hyperintensity, *n* (%)	
Fazekas 0	62 (24)
Fazekas 1	97 (38)
Fazekas 2	66 (26)
Fazekas 3	29 (11)
Acute ischemic stroke treatment, *n* (%)	
Single antiplatelet	118 (47)
Dual antiplatelet	89 (35)
Anticoagulant	34 (13)
Intravenous alteplase	4 (2)
Others	9 (3)

NIHSS, National Institutes of Health Stroke Scale; TIA, transient ischemic attack; LAA, large-artery atherosclerosis; SAO, small-artery occlusion; CE, cardioembolism; UND, undetermined cause; OC, other defined cause.

Table 2. Outcomes of patients with small ischemic stroke and high-risk TIA

Outcomes	*n* (%)
At 3 months	
Favorable outcome (mRS0-1)	175 (69)
Recurrent stroke	11 (4)
Intracerebral hemorrhage	1
Ischemic stroke	10
Distribution of mRS	
0	97 (38)
1	78 (31)
2	37 (15)
3	27 (11)
4	8 (3)
5	4 (2)
6	3 (1)
At final follow-up (median 22 months)	
Favorable outcome (mRS0-1)	173 (68)
Recurrent stroke	31 (12)
Intracerebral hemorrhage	3
Ischemic stroke	28
Distribution of mRS	
0	123 (48)
1	50 (20)
2	33 (13)
3	26 (10)
4	5 (2)
5	7 (3)
6	10 (4)

Results

There were 297 patients with mild stroke or high-risk TIA, who were admitted to stroke unit during the study period, accounting for 37% (297/807 patients) of total ischemic stroke admissions. Eighteen patients were excluded due to participation in an antithrombotic trial. Twenty-five patients missed follow-up. There were 230 patients with mild ischemic stroke and 24 patients with TIA. Baseline characteristics of 254 patients are presented in Table 1. Although small artery occlusion (SAO) was the most common cause of stroke (53%), large artery atherosclerosis (LAA) and cardioembolism (CE) were found to be the causes in 18% and 17%, respectively. For the acute treatment, single antiplatelet was prescribed in 47% of the patients, dual antiplatelet in 35%, anticoagulant in 13%, and intravenous thrombolysis in 2% of the patients. Mean duration of hospital stay was 4 days (range from 1 to 26 days). The outcomes of the patients at 3 months and at final follow-up, median 22 months, are presented in Table 2.

Clinical Progression during Admission

During admission, 38 patients (15%) had clinical progression. Mean NIHSS scores at admission and at progression were 3.5 (range from 1 to 5) and 6.1 (range from 2 to 12), respectively. Patients with clinical progression

Table 3. Factors associated with clinical progression from univariate analysis

Baseline characteristics	No progression (*N* = 216)	Progression (*N* = 38)	*p* value
Mean age, years	64	68	0.074
Age <70 years, *n* (%)	137 (63)	19 (50)	
Age ≥70 years, *n* (%)	79 (37)	19 (50)	0.117
Male sex, *n* (%)	149 (69)	22 (58)	0.179
Mean NIHSS on admission	3.023	3.5	0.058
Previous status, *n* (%)			
Independent (mRS0-2)	203 (94)	32 (84)	
Walk with instruments/dependent (mRS3-5)	13 (6)	6 (16)	0.035
Hypertension	164 (76)	26 (68)	0.326
Diabetes mellitus	75 (35)	14 (37)	0.801
Hyperlipidemia	110 (51)	27 (71)	0.022
Coronary artery disease	27 (13)	2 (5)	0.196
History of stroke	43 (20)	9 (24)	0.595
History of ICH	7 (3)	1 (3)	0.843
Atrial fibrillation	25 (12)	9 (24)	0.043
Smoking	52 (24)	6 (16)	0.262
Stroke subtypes, *n* (%)			
LAA	33 (17)	8 (21)	
SAO	107 (56)	15 (40)	
CE	28 (15)	11 (29)	
UND	23 (12)	4 (11)	
Other causes	1 (0.5)	0	0.049
Stroke location, *n* (%)			
Cortical lesion	44 (23)	7 (18)	
Subcortical lesion	86 (45)	12 (32)	
Brainstem/cerebellum	43 (22)	15 (40)	
Multiple-territory infarct	19 (10)	4 (11)	0.139
Fazekas, *n* (%)			
0–1	136 (63)	23 (61)	
2–3	80 (37)	15 (40)	0.775
Acute treatment, *n* (%)			
Single antiplatelet	103 (48)	15 (40)	
Dual antiplatelet	79 (37)	10 (26)	
Anticoagulant	23 (11)	11 (29)	
Intravenous alteplase	3 (1)	1 (3)	
Others	8 (4)	1 (3)	0.074
Recurrent stroke, *n* (%)	27 (13)	4 (11)	0.772
Favorable outcome at 90 days, *n* (%)	167(77)	8 (21)	<0.001

had a higher proportion of dependence prior to the index stroke, more hyperlipidemia, and atrial fibrillation (Table 3). For the causes of stroke, LAA (8/38; 21%) and CE (11/38; 29%) were more frequent in those with clinical progression. Brainstem/cerebellum stroke (15/38; 40%) was also commonly found in these patients. Multivariate analysis showed that LAA (OR 2.49, 95% CI: 1.06–5.81, *p* value = 0.035), CE (OR 3.34, 95% CI: 1.26–8.87, *p* value = 0.015), and brainstem stroke (OR 2.78, 95% CI: 1.28–6.01, *p* value = 0.009) were related to clinical progression. Patients, who had clinical progression during admission, had less favorable outcome at 90 days (21% vs. 77%, *p* value < 0.001).

Clinical Outcomes

At 3 months, 175 patients (69%) had favorable outcomes (Table 4). At the final follow-up, median 22 months, 173 patients (68%) had favorable outcomes and 81 patients had unfavorable outcomes. Ten patients died (3 patients with CE, 3 patients with undetermined cause (UND), 2 patients with LAA, 1 patient with SAO, and another with TIA). The causes of death were sepsis (7 pa-

Table 4. Factors associated with unfavorable outcomes at final follow-up from univariate analysis

Baseline characteristics	Favorable outcome (*N* = 173)	Unfavorable outcome (*N* = 81)	*p* value
Mean age, years	61	71	<0.001
Male sex, *n* (%)	120 (69)	51 (63)	0.311
Mean NIHSS on admission	2.9	3.6	<0.001
Previous status, *n* (%)			
Independent (mRS0-2)	171 (99)	64 (79)	
Walk with instruments/dependent (mRS3-5)	2 (1)	17 (21)	<0.001
Hypertension	126 (73)	64 (79)	0.29
Diabetes mellitus	58 (34)	31 (38)	0.46
Hyperlipidemia	88 (51)	49 (61)	0.151
Coronary artery disease	17 (10)	12 (15)	0.244
History of stroke	30 (17)	22 (27	0.071
Atrial fibrillation	18 (10)	16 (20)	0.041
Smoking	45 (26)	13 (16)	0.078
Stroke subtypes, *n* (%)			
LAA	14 (9)	27 (33)	
SAO	99 (66)	23 (29)	
CE	20 (13)	19 (24)	
UND	16 (11)	11 (14)	
Other causes	1 (1)	0	0. 091
Stroke location, *n* (%)			
Cortical lesion	32 (21)	19 (23)	
Subcortical lesion	68 (45)	30 (38)	
Brainstem/cerebellum	37 (25)	21 (26)	
Multiple-territory infarct	13 (9)	10 (12)	0.408
Fazekas, *n* (%)			
0–1	126 (73)	33 (41)	
2–3	47 (27)	48 (59)	<0.001
Acute treatment, *n* (%)			
Single antiplatelet	80 (46)	38 (47)	
Dual antiplatelet	66 (38)	23 (28)	
Anticoagulant	19 (11)	15 (19)	
Intravenous alteplase	3 (2)	1 (1)	
Others	5 (3)	4 (5)	0.2
Clinical progression during admission, *n* (%)	12 (7)	26 (32)	<0.001
Recurrent stroke, *n* (%)	9 (5)	22 (27)	0.02

tients), intraventricular hemorrhage (1 patient), and unknown (2 patients). Patients who had unfavorable outcomes were older and had slightly more severe stroke, lower proportion of independence prior to stroke, more atrial fibrillation, more severe white matter lesions, clinical progression during admission, and recurrent stroke (Table 4). Multivariate analysis showed that previous disability (OR 1.81, 95% CI: 3.31–100, p value = 0.001), moderate to severe white matter lesions (OR 2.90, 95% CI: 1.44–5.84, p value = 0.003), clinical progression (OR 12.5, 95% CI: 5.08–31.25, p value < 0.001), and recurrent stroke (OR 8.47, 95% CI: 3.21–22.72, p value < 0.001) were related to unfavorable outcomes at final follow-up.

Recurrent Stroke

Eleven patients (4%) had recurrent stroke within 3 months; 10 patients with ischemic stroke, and one with intracerebral hemorrhage. The total cases of recurrent stroke at the final follow-up (median 22 months) were 31(12%); thus, 65% of recurrence occurred during 3–22 months. Patients with recurrent stroke had less favorable outcome as compared to those without (32% vs. 73%, p value < 0.001). Univariate analysis showed that patients with recurrent stroke were older, more often male, with diabetes mellitus, history of intracerebral hemorrhage, atrial fibrillation, and smoking (Table 5). Only the variables of older age (≥70 years) (OR 6.68, 95% CI: 2.35–

Table 5. Factors associated with recurrent stroke at final follow-up from univariate analysis

Baseline characteristics	No recurrent (*N* = 223)	Recurrent stroke (*N* = 31)	*p* value
Mean age, *n* (%), years	63	72	
Age <70 years	147 (66)	9 (29)	
Age ≥70 years	76 (34)	22 (71)	<0.001
Male sex, *n* (%)	145 (65)	26 (84)	0.035
Mean NIHSS on admission	3.08	3.16	0.74
Previous status, *n* (%)			
Independent (mRS0-2)	209 (94)	26 (84)	
Walk with instruments/dependent (mRS3-5)	14 (6)	5 (16)	0.052
Hypertension	166 (75)	24 (77)	0.75
Diabetes mellitus	73 (33)	16 (52)	0.041
Hyperlipidemia	118 (53)	19 (61)	0.394
Coronary artery disease	26 (12)	3 (10)	0.739
History of stroke	45 (20)	7 (23)	0.766
History of ICH	5 (2)	3 (10)	0.027
Atrial fibrillation	25 (11)	9 (29)	0.005
Smoking	47 (21)	11 (36)	0.045
Stroke subtypes, *n* (%)			
LAA	33 (17)	8 (27)	
SAO	113 (57)	9 (30)	
CE	30 (15)	9 (30)	
UND	23 (12)	4 (13)	
Other causes	1 (0.5)	0	0.154
Stroke location, *n* (%)			
Cortical lesion	44 (22)	7 (23)	
Subcortical lesion	87 (44)	11 (37)	
Brainstem/cerebellum	52 (26)	6 (20)	
Multiple-territory infarct	17 (9)	6 (20)	0.264
Fazekas, *n* (%)			
0–1	143 (64)	16 (52)	
2–3	80 (36)	15 (48)	0.183
Acute treatment, *n* (%)			
Single antiplatelet	104 (47)	14 (45)	
Dual antiplatelet	81 (37)	8 (26)	
Anticoagulant	26 (11)	8 (26)	
Intravenous alteplase	3 (1)	1 (3)	
Others	9 (4)	0	0.208
Clinical progression during admission	34 (15)	4 (13)	0.772

19.02, p value < 0.001), diabetes mellitus (OR 2.59, 95% CI: 1.07–6.27, p value = 0.034), and smoking (OR 4.26, 95% CI: 1.52–11.95, p value = 0.006) were related to recurrent stroke from multivariate analysis.

Discussion

Patients with mild stroke and high-risk TIA in our study accounted for 37% of all admitted ischemic stroke patients. The number was lower than in a previous study (>50%) [1]. This might be explained by our center being a referral center; thus, greater proportion of patients with moderate to severe stroke were referred to have acute intervention treatment.

From previous studies, clinical worsening occurred in 20–37% of the unselected patients with ischemic stroke [17, 18]. Three main causes were found which were (1) medical complications, especially infection; (2) brain edema, commonly found in large strokes; and (3) gradual or stepwise increases in focal neurological deficits [17]. However, in patients with mild stroke, where small infarct lesions were expected, the incidence of clinical progression and the causes would be different. Clinical pro-

gression during admission was found in 15% of the patients in our study, mainly from gradual or stepwise increases in focal deficits. LAA, CE, and brainstem stroke were related to clinical progression. A previous study revealed that progression was commonly found in patients with lacunar infarcts (37%) and large artery occlusive disease (33%) [18]. Hypoperfusion and distal embolization were proposed as the main mechanisms of worsening in patients with severe stenosis or occlusion of large and penetrating artery disease. Twenty percent of patients with emboli arising from heart or aorta worsened during 24–48 h, related to distal emboli [17].

Patients with mild stroke and TIA are expected to have favorable outcomes. However, unfavorable outcomes were reported in 12.3–39% from previous studies, and old age, diabetes, limb motor disturbance, ataxia, baseline NIHSS, early worsening, recurrent stroke, medical complications, and heart disease (myocardial infarction) were related to the poor outcomes [3, 19, 20]. Our study showed that 81 patients (32%) had unfavorable outcomes at the final follow-up (median 22 months), which was related to previous disability, moderate to severe white matter lesions, clinical progression, and recurrent stroke. White matter lesions have been reported to be related to poor outcomes in mild stroke patients [21]. The white matter lesions were likely a cause of chronic cerebrovascular injury, and its burden may signify a diminished capacity of cerebral tissue to tolerate ischemia [22]. Thus, a small new stroke on top of significant white matter lesions could cause decompensation and lead to poor outcomes in patients.

Implementation of early assessment and management of patients with mild ischemic stroke and high-risk TIA in clinical practice may improve clinical outcomes of these patients. Several landmark trials reported the rate of recurrent stroke in patients with mild stroke and/or TIA [4, 13, 23]. However, there were some differences in baseline characteristics of included patients among studies. In 2016, the TIAregistry.org project, in which the majority of the patients was TIA (67%) and 78% of the patients were evaluated by a stroke specialist within 24 h, reported the risk of recurrent stroke as 1.5% at 2 days, 2.1% at 7 days, and 3.7% at 90 days after symptom onset [13]. The CHANCE study, published in 2013, including Chinese patients with noncardioembolic, minor stroke (72%) or high-risk TIA (28%), reported that 3-week dual antiplatelet (aspirin plus clopidogrel) treatment within 24 h of stroke onset significantly reduced the risk of recurrent stroke at 90 days of follow-up as compared to the aspirin group (8.2% vs. 11.7%, p value < 0.001) [4]. The POINT study, published in 2018, including mainly Western patients with noncardioembolic, minor stroke (57%) or high-risk TIA (43%), reported that dual antiplatelet (aspirin plus clopidogrel) within 12 h of stroke onset also reduced the risk of recurrent stroke at 90 days of follow-up as compared to aspirin alone (4.6% vs. 6.3%, p value = 0.001) [23].

Our study included patients with mild stroke and high-risk TIA from various causes of stroke, which was commonly found in routine clinical practice. Different regimens of acute treatment were prescribed. Thus, the outcomes of treatment might not be comparable to the landmark trials, which included the particular group of patients with noncardioembolic stroke and used the fixed medication regimens. Wu et al. [8] reported the rate of recurrent stroke of 9.8% in patients with minor stroke (NIHSS1-3) from the China National Stroke Registry. They included patients between September 2007 and August 2008 and time from onset to admission less than 24 h in about half of the patients in the study. LAA was the most common stroke subtype (approximate 43%). This might explain higher rate of recurrent stroke than our study. All patients in our study were evaluated by a stroke specialist within 24 h, and all received acute treatment per protocol. The rate of recurrent stroke within 90 days was comparable to the 2016 TIAregistry.org project. However, at beyond 3 months, besides the patients' factors, such as noncompliance in some patients, or emerging of atrial fibrillation, or concomitant medical conditions, the treatment for secondary prevention of stroke varied depending on the neurologists who followed the patients, such as the dose of aspirin or types of oral anticoagulant. This might explain the slightly higher rate of recurrent stroke during follow-up.

This study evaluated the different aspects of outcomes, including progressive stroke, 3-month and long-term clinical outcomes, and recurrent stroke, in patients with mild ischemic stroke and high-risk TIA from current clinical practice. However, there were some limitations. First was the study conducted in a single center with small sample numbers. The result of the study might not represent the data from other centers. Second, 25 patients lost follow-up after being discharged from the hospital. Third, the main long-term outcomes of interest were recurrent stroke and death, not the composite outcome of cardiovascular events and death.

The advanced knowledge over the past decades led to some changes in management of patients with high-risk TIA or minor stroke. Aggressive and/or specific medical treatment for primary/secondary stroke prevention, early

assessment, and specific management per the causes of stroke were applied. This would provide the better outcomes and reduce the risk of recurrent stroke. In conclusion, implementation of the up-to-date standard care in clinical practice would bring good clinical outcomes to the patients with mild stroke and high-risk TIA.

Statement of Ethics

The study has been granted an exemption from requiring written informed consent and was approved by the Human Ethic Committee of Thammasat University (project number: MTU-EC-IM-2-257/63).

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Apiluk Wesanonthawech: data collection and reviewing manuscript; Pornpatr A. Dharmasaroja: study design, data collection, data analysis, writing manuscript, and submission.

Data Availability Statement

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

References

1 Reeves M, Khoury J, Alwell K, Moomaw C, Flaherty M, Woo D, et al. Distribution of National Institutes of Health Stroke Scale in the Cincinnati/Northern Kentucky Stroke Study. Stroke. 2013;44(11):3211–3.
2 Powers WJ, Rabinstein AA, Ackerson T, Adeoye OM, Bambakidis NC, Becker K, et al. Guidelines for the early management of patients with acute ischemic stroke: 2019 update to the 2018 guidelines for the early management of acute ischemic stroke. A guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke. 2019;50(12):e344–418.
3 Cucchiara B, George DK, Kasner SE, Knutsson M, Denison H, Ladenvall P, et al. Disability after minor stroke and TIA a secondary analysis of the SOCRATES trial. Neurology. 2019;93(7):e708–16.
4 Wang Y, Wang Y, Zhao X, Liu L, Wang D, Wang C, et al. Clopidogrel with aspirin in acute minor stroke or transient ischemic attack. N Engl J Med. 2013;369(1):11–9.
5 Kleindorfer DO, Towfighi A, Chaturvedi S, Cockroft KM, Gutierrez J, Lombardi-Hill D, et al. 2021 Guideline for the Prevention of Stroke in Patients with Stroke and Transient Ischemic Attack: a Guideline from the American Heart Association/American Stroke Association. Stroke. 2021;52(7):e364–467.
6 Johnston SC, Gress DR, Browner WS, Sidney S. Short-term prognosis after emergency department diagnosis of TIA. JAMA. 2000;284(22):2901–6.
7 Lovett JK, Dennis MS, Sandercock PAG, Bamford J, Warlow CP, Rothwell PM. Very early risk of stroke after a first transient ischemic attack. Stroke. 2003;34(8):e138–40.
8 Wu L, Wang A, Wang X, Zhao X, Wang C, Liu L, et al. Factors for short-term outcomes in patients with a minor stroke: results from China National stroke registry. BMC Neurol. 2015;15:253.
9 Wu CM, McLaughlin K, Lorenzetti DL, Hill MD, Manns BJ, Ghali WA. Early risk of stroke after transient ischemic attack: a systematic review and meta-analysis. Arch Intern Med. 2007;167(22):2417–22.
10 Johnston SC, Rothwell PM, Nguyen-Huynh MN, Giles MF, Elkins JS, Bernstein AL, et al. Validation and refinement of scores to predict very early stroke risk after transient ischaemic attack. Lancet. 2007;369(9558):283–92.
11 Rothwell PM, Giles MF, Chandratheva A, Marquardt L, Geraghty O, Redgrave JNE, 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(9596):1432–42.
12 Giles MF, Rothwell PM. Risk of stroke early after transient ischaemic attack: a systematic review and meta-analysis. Lancet Neurol. 2007;6(12):1063–72.
13 Amarenco P, Lavallee PC, Labreuche J, Albers GW, Bornstein NM, Canhao P, et al. One-year risk of stroke after transient ischemic attack or minor stroke. N Engl J Med. 2016;374(16):1533–42.
14 The European Stroke Organization (ESO) Executive Committee and the ESO Writing Committee. Guidelines for management of ischemic stroke and transient ischemic attack 2008. Cerebrovasc Dis. 2008;25:457–507.
15 National Institute for Health and Care Excellence (UK). Stroke and transient ischaemic attack in over 16s: diagnosis and initial management. 2019 May. http://www.nice.org.uk/guidance/cg68.
16 Tantirithisak T, Hanchaiphiboolkul S, Towanabut S, et al. Clinical practice guidelines for ischemic stroke. Bangkok, Thailand: Thanaplace; 2019.
17 Caplan LR. Worsening in ischemic stroke patients: is it time for a new strategy? Stroke. 2002;33(6):1443–5.
18 Mohr JP, Caplan LR, Melski JW, Goldstein RJ, Duncan GW, Kistler JP, et al. The Harvard Cooperative Stroke Registry: a prospective registry. Neurology. 1978;28(8):754–62.
19 You W, Li Y, Ouyang J, Li H, Yang S, Hu Q, et al. Predictors of poor outcome in patients with minor ischemic stroke by using magnetic resonance imaging. J Mol Neurosci. 2019;69(3):478–84.
20 Sangha RS, Caprio FZ, Askew R, Corado C, Bernstein R, Curran Y, et al. Quality of life in patients with TIA and minor ischemic stroke. Neurology. 2015;85(22):1957–63.
21 Onteddu SR, Goddeau RP Jr, Minaeian A, Henninger N. Clinical impact of leukoaraiosis burden and chronological age on neurological deficit recovery and 90-day outcome after minor ischemic stroke. J Neurol Sci. 2015;359(1–2):418–23.
22 Zerna C, Yu AYX, Modi J, Patel SK, Coulter JI, Smith EE, et al. Association of white matter hyperintensities with short-term outcomes in patients with minor cerebrovascular events. Stroke. 2018;49(4):919–23.
23 Johnston SC, Easton JD, Farrant M, Barsan W, Conwit RA, Elm JJ, et al. Clopidogrel and aspirin in acute ischemic stroke and high-risk TIA. N Engl J Med. 2018;379(3):215–25.