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ORIGINAL ARTICLE

Revisiting the role of TEG-PM in stroke prevention by drug selection for mono-antiplatelet medication following dual-antiplatelet treatment.

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Abstract

BACKGROUNDS: Dual-antiplatelet therapy (DAPT) with aspirin and clopidogrel for minor strokes or TIAs has been demonstrated in several RCTs. Whether drug selection for mono-antiplatelet therapy (MAPT) following DAPT may influence stroke recurrence has not been clarified, especially for patients with intracranial atherosclerosis stenosis (ICAS). The Thrombelastography Platelet Mapping (TEG-PM) assay claimed to be capable of monitoring platelet function secondary to antiplatelet therapy.

PURPOSE: The aim of this study was to investigate the preventive role of TEG-PM in individualized drug selection for MAPT following DAPT in patients with minor stroke or TIA.

METHODS: We retrospectively reviewed our patient database to identify individuals with minor stroke or TIA between February 2019 and July 2022. Patients were divided into ICAS and non-ICAS groups, and the efficacy and safety of TEG-PM-guided MAPT for stroke prevention after minor stroke or TIA were investigated in each group.

RESULTS: ICAS patients with TEG-PM-guided MAPT had lower rates of recurrent stroke than patients without TEG-PM guidance during a mean follow-up period of 18.1 months (6.3% vs 15.2%; $p = 0.04$). Patients without ICAS also tended to benefit from TEG-PM-guided MAPT with lower rates of stroke recurrence (2.6% vs 8.7%; $p = 0.02$). No difference in the safety outcome of any bleeding events was observed in patients with TEG-PM-guided MAPT and those without (ICAS group, 2.1% vs 3.0%; $p = 0.68$; non-ICAS group, 1.3% vs 2.3%; $p = 0.79$).

CONCLUSION: The TEG-PM could be a tangible preprocessing in drug selection for MAPT following DAPT in patients with minor strokes or TIAs, especially for those with non-stented ICASs.

Abbreviations:

DAPT	- Dual-Antiplatelet Therapy
MAPT	- Mono-Antiplatelet Therapy
ICAS	- Intracranial Atherosclerosis Stenosis
TEG-PM	- The Thrombelastography Platelet Mapping
TIA	- Transient Ischemic Attack
LPR	- Low Platelet Reactivity
PFT	- Platelet Function Test
MRI	- Magnetic Resonance Imaging
MRA	- Magnetic Resonance Angiography
WASID	- Warfarin and Aspirin for Symptomatic Intracranial Disease
NIHSS	- National Institutes of Health Stroke Scale
ADP	- Adenosine Diphosphate
AA	- Arachidonic Acid

INTRODUCTION

The prevention and treatment of every ischemic brain event is not always associated with the patient's return to a full-fledged life and brings suffering not only for him but also for his family. Therefore, the search for optimal treatment and prevention of repeated events has an irreplaceable place in this group of patients. Dual-antiplatelet therapy (DAPT) with aspirin and clopidogrel has been demonstrated in the management of acute minor ischemic stroke and transient ischemic attack (TIA) (Kernan *et al.* 2014; Wang *et al.* 2013; Wang *et al.* 2017). Although the optimal duration of DAPT varied in the literature, according to national guidelines in various regions, the mono-antiplatelet treatment (MAPT) following DAPT has been strongly recommended for the secondary prevention of stroke, especially in patients with an etiology of intracranial atherosclerosis stenosis (ICAS) (Ge *et al.* 2016; Johnston *et al.* 2018; Mehndiratta *et al.* 2014; Wang *et al.* 2013). Currently, specific drug selection strategies for a long-term MAPT agent after DAPT has not been established, the choice was often randomly made by the clinician or patient without a clear rationale (Wang *et al.* 2015). One explanation is that, to date, it remains unclear whether drug screening could benefit patients who accept MAPT secondary to DAPT in real-world practice. However, even after a sufficiently long DAPT (e.g., 90 days), a certain proportion of patients, especially those with ICAS, could experience recurrent ischemic stroke during the subsequent MAPT phase (Chimowitz *et al.* 2011; Sangha *et al.* 2017; Wang *et al.* 2015).

Although stroke recurrence remains a complex and multifactorial issue encompassing both genetic and environmental factors, low platelet reactivity (LPR) may play an important role in response to antiplatelet agents, particularly among certain ethnic groups (e.g., clopidogrel for Asians) (Aradi *et al.* 2015; Stone *et al.* 2013; Wang *et al.* 2016). Therefore, patients who selected mono-platelet aggregation inhibitors randomly may harbor more stroke recurrent risk than those undergoing a platelet function test (PFT) to guide individualized antiplatelet medication (Trenk *et al.* 2008). Recently, multiple PFTs (e.g., LTA, VASP, TEG-PM) have been practically used in the clinical setting to monitor platelet inhibition secondary to antiplatelet therapy (Fontana *et al.* 2020). However, no substantial evidence has been reached on one of these methods for the optimal selection of a MAPT agent after DAPT for patients with minor stroke and TIA. In this retrospective study, we aimed to investigate the significance of a TEG-PM-guided selection in MAPT medication following DAPT, thus addressing the potential importance of a tailored MAPT strategy for stroke-recurrence prevention after minor strokes or TIAs, especially for ICASs.

MATERIALS AND METHODS

Patients and group

This study was a single-institution retrospective study conducted at The China and Japan Union Hospital of Jilin University. We retrospectively reviewed our patient database to identify individuals with minor stroke or TIA (≤24 hours of onset) between February 2019 and July 2022. All the patients underwent magnetic resonance imaging (MRI) and magnetic resonance angiography (MRA) of brain. Based on the results of MRA, the patients were classified into non-ICAS and ICAS groups. Each group was divided into 2 subgroups: non-TEG-PM-guided and TEG-PM-guided. Minor stroke was defined by a National Institutes of Health Stroke Scale (NIHSS) Score of ≤ 3 at the time of treatment (Fischer *et al.* 2010). TIA was defined as a transient episode of neurological deficits caused by the focal brain without acute infarction on DWI (Easton *et al.* 2009). Intracranial atherosclerosis stenosis (ICAS) was defined as 50% to 99% stenosis of the lumen diameter or occlusion of at least one of the following arterial segments on 3D time-of-flight MRA: intracranial portion of internal carotid arteries, middle cerebral arteries (M1), intracranial portion of vertebral arteries, and basilar artery. The degree of stenosis was determined using the WASID (Warfarin and Aspirin for Symptomatic Intracranial Disease) criteria (Chimowitz *et al.* 2005). The baseline demographic and clinical characteristics of each group were recorded. Informed consent was obtained from all patients or legal guardians, and ethical approval for this study was granted by the local review board of China and Japan Union Hospital of Jilin University (No.2020-NSFC-087). The clinical and imaging data were examined by two neurologists (M.J. and Y.L.) independently, who were blind to treatments.

Inclusion/Exclusion Criteria

Inclusion criteria: age≥40; diagnosis of acute minor ischemic stroke (NIHSS score≤3) or moderate to high-risk TIA ($ABCD^2$ score≥4); receive antiplatelet aggregation within 24 hours after the symptom.

Exclusion criteria: mild or indeterminate neurological deficits without evidence of acute infarction on MRI of the head; highly suspected cardioembolic stroke

Tab. 1. Tailored strategy for TEG-PM-guided MAPT following DAPT

TEG-PM results	MAPT agent selection
ADP inhibition >30%, AA inhibition≤50%	clopidogrel 75 mg/day
ADP inhibition ≤ 30%, AA inhibition >50%	aspirin 100 mg/day
ADP inhibition ≤ 30%, AA inhibition ≤ 50%	cilostazol 100 mg 2×/day
ADP inhibition > 30%, AA inhibition >50%	the one with a higher inhibition rate

or other nonischemic diseases, such as brain infection, vascular malformation, tumor; anticoagulation therapy before stroke onset or definite indication for anticoagulation; presence of peptic ulceration or history of bleeding diathesis; platelet count <100,000/mm or coagulopathy; major surgery or trauma in the previous 3 months; coexisting severe systemic diseases, such as terminal malignancy or serious renal or liver disease; pregnancy, breastfeeding, or planned pregnancy during the trial; known contraindication to clopidogrel or aspirin; treated with thrombolysis; modified Rankin Scale>2.

Medication

All patients received a 300 mg loading dose of clopidogrel and 100 mg aspirin within 24 hours after the onset of symptoms. The DAPT (75 mg clopidogrel and 100 mg aspirin/day) continued for up to 21 days and 90 days in the non-ICAS group and ICAS group, respectively. Thereafter, a tailored MAPT was performed in the TEG-PM-guided group (Table 1), and the drug of MAPT used in the control group was randomly selected by the clinician or the patients (Wang *et al.* 2015).

TEG-PM assay

The TEG-PM was measured on the (6.8±2.3) day of the DAPT. Blood samples (3-4ml) were drawn from the previously uncannulated antecubital vein and collected in a blood collection tube containing 75 USP lithium heparin (Becton drive, USA), inverted gently three to five times for mixing, and then sent immediately to the laboratory for analyzing blood according to the manufacturer's protocol (Haemoscope). The degree of platelet inhibition to P2Y12 receptor or cyclooxygenase (COX) pathways can be measured by the addition of adenosine diphosphate (ADP) agonists or arachidonic acid (AA). AA/ADP channel inhibition rate (%)=[($MA_{AA/ADP}$−MA_{fibrin})/($MA_{thrombin}$−MA_{fibrin})]×100% (Tantry *et al.* 2005). MA_{AA} (AA-induced clot strength) and MA_{ADP} (ADP-induced clot strength) were used to measure the effects of aspirin and clopidogrel, respectively.

Outcomes assessment

The primary efficacy endpoint was a new ischemic and hemorrhagic stroke event observed during the follow-up period. The secondary efficacy endpoints were ischemic stroke, TIA, myocardial infarction, hemorrhagic stroke, vascular death, or composites of major vascular events during the follow-up period. Ischemic stroke was defined as an acute focal infarction of the brain or retina with one of the following: sudden onset of a new focal neurologic deficit, with clinical or imaging evidence of infarction lasting 24 hours or more and not attributable to a nonischemic cause. Vascular death was defined as death from stroke, myocardial infarction, arrhythmia, pulmonary embolism, or other vascular causes or sudden unexpected death (Wang *et al.* 2013). Composites of major vascular events including stroke, myocardial infarction, or vascular death.

The safety endpoint was moderate-to-severe bleeding events during the follow-up period defined by the GUSTO criteria (The GUSTO investigators, 1993). Severe bleeding was defined as fatal or intracranial hemorrhage or other hemorrhage causing hemodynamic compromise that required blood or fluid replacement, inotropic support, or surgical intervention. Moderate bleeding was defined as bleeding that required a transfusion of blood but did not lead to a hemodynamic compromise requiring intervention (The GUSTO investigators, 1993). Follow-up information was obtained by telephone interviews or outpatient visits.

Statistical analysis

Continuous variables were expressed as median with interquartile range, comparisons between groups were performed using Mann-Whitney U-test. Categorical variables were presented as counts and percentages. The $\chi 2$ test or the Fisher exact test was performed for the comparison of categorical variables between two groups. Cox proportional risk models were used to assess differences in endpoint events across groups during the follow-up period. When multiple events of the same type exist, the first occurrence time of the event was selected in the model. We performed separate subgroup analysis of patients who received or did not receive TEG-PM-guided. $p < 0.05$ was considered statistically significant. Clinical data were recorded and tabulated using Microsoft Excel software. All statistical analyses were performed with SPSS software (Version 26.0).

RESULTS

Patients

From February 2019 to July 2022, 521 patients with minor ischemic stroke or TIA were included, with

195 (37.4%) in the ICAS group and 326 (62.6%) in the non-ICAS group; 249 (47.8%) in the TEG-PM-guided group and 272 (52.2%) in the non-TEG-PM-guided group. A total of 15 patients (2.9%) were lost to follow-up, with 8 in the TEG-PM-guided group and 7 in the non-TEG-PM-guided group. Except for age, there were no significant differences between groups in baseline characteristics. (Table 2)

Primary efficacy outcome

During a mean follow-up of 18.1 months, stroke occurred in 10 patients (4.0%) and 30 patients (11.0%) in the TEG-PM-guided group and the Non-TEG-PM-guided group, irrespective of the presence of ICAS (HR: 0.39; 95% [CI]: 0.19-0.78; $p < 0.005$). Among patients with non-stented ICAS, stroke occurred in 6 patients (6.3%) in the TEG-PM-guided subgroup compared with 15 patients (15.2%) in the Non-TEG-PM-guided subgroup (HR: 0.39; 95% [CI]: 0.16-0.93; $p = 0.03$). Three new strokes (3.1%) were fatal or disabling in the TEG-PM-guided subgroup, compared with 11 (11.1%) in the non-TEG-PM-guided subgroup (HR: 0.28; 95% [CI]: 0.09-0.98; $p = 0.03$).

For patients without ICAS, stroke occurred in 4 patients (2.6%) in the TEG-PM-guided subgroup compared with 15 patients (8.7%) in the

Tab. 2. Baseline characteristics of the patients

Characteristic	ICAS (n=195)			Non-ICAS (n=326)			*p*-value[b]
	TEG-PM-guided	Non-TEG-PM-guided	*p*-value[a]	TEG-PM-guided	Non-TEG-PM-guided	*p*-value[a]	
Patients, n	96	99		153	173		
Age, y, median (IQR)	61 (56-68)	65 (58-69)	0.13	60 (52.5-66)	61 (55.5-68.5)	0.08	0.003
Gender, n (%)			0.65			0.56	0.59
Male	67 (69.8)	72 (72.7)		108 (70.6)	117 (67.6)		
Female	29 (30.2)	27 (27.3)		45 (29.4)	56 (32.4)		
Medical history, n (%)							
Ischemic stroke	24 (25.0)	23 (23.2)	0.77	32 (20.9)	39 (22.5)	0.72	0.54
TIA	3 (3.1)	0 (0)	0.23	5 (3.3)	2 (1.2)	0.35	0.87
Hypertension	67 (69.8)	71 (71.7)	0.77	104 (68.0)	119 (69.2)	0.81	0.61
Diabetes mellitus	30 (31.3)	33 (33.3)	0.76	38 (24.8)	45 (26.2)	0.78	0.10
Hypercholesterolemia	14 (14.6)	15 (15.2)	0.91	21 (13.7)	27 (15.7)	0.62	0.98
Myocardial infarction	2 (2.1)	4 (4.0)	0.71	5 (3.3)	3 (1.7)	0.59	0.67
Angina	3 (3.1)	2 (2.0)	0.97	6 (3.9)	8 (4.6)	0.76	0.31
Heart failure	1 (1.0)	2 (2.0)	1.00	1 (0.7)	3 (1.7)	0.70	1.00
Atrial fibrillation	2 (2.1)	5 (5.1)	0.47	1 (0.7)	5 (2.9)	0.28	0.34
Valvular heart disease	3 (3.1)	1 (1.0)	0.59	5 (3.3)	8 (4.6)	0.53	0.23
Smoking	54 (56.3)	57 (57.6)	0.85	78 (51)	89 (51.7)	0.89	0.22
Drinking	38 (39.6)	36 (36.4)	0.64	49 (32)	58 (33.7)	0.75	0.24
Ischemic event, n (%)			0.11			0.08	0.31
TIA	12 (12.5)	21 (21.2)		25 (16.3)	42 (24.3)		
Minor stroke	84 (87.5)	78 (78.8)		128 (83.7)	131 (75.7)		
Inpatient medications, n (%)							
Antihypertensive	45 (46.9)	50 (50.5)	0.61	72 (47.1)	78 (45.1)	0.72	0.55
Antidiabetic	19 (19.8)	22 (22.2)	0.68	26 (17.0)	33 (19.1)	0.63	0.41
Incidence of drug resistance, n (%)							
Only Aspirin match	27 (28.1)			42 (27.5)			0.91
Only Clopidogrel match	2 (2.1)			6 (3.9)			0.67
All match	64 (66.7)			96 (62.7)			0.53
None match	3(3.1)			9 (5.9)			0.49

[a] Comparisons between TEG-PM-guided and Non-TEG-PM-guided groups.
[b] Comparisons between ICAS and Non-ICAS groups.

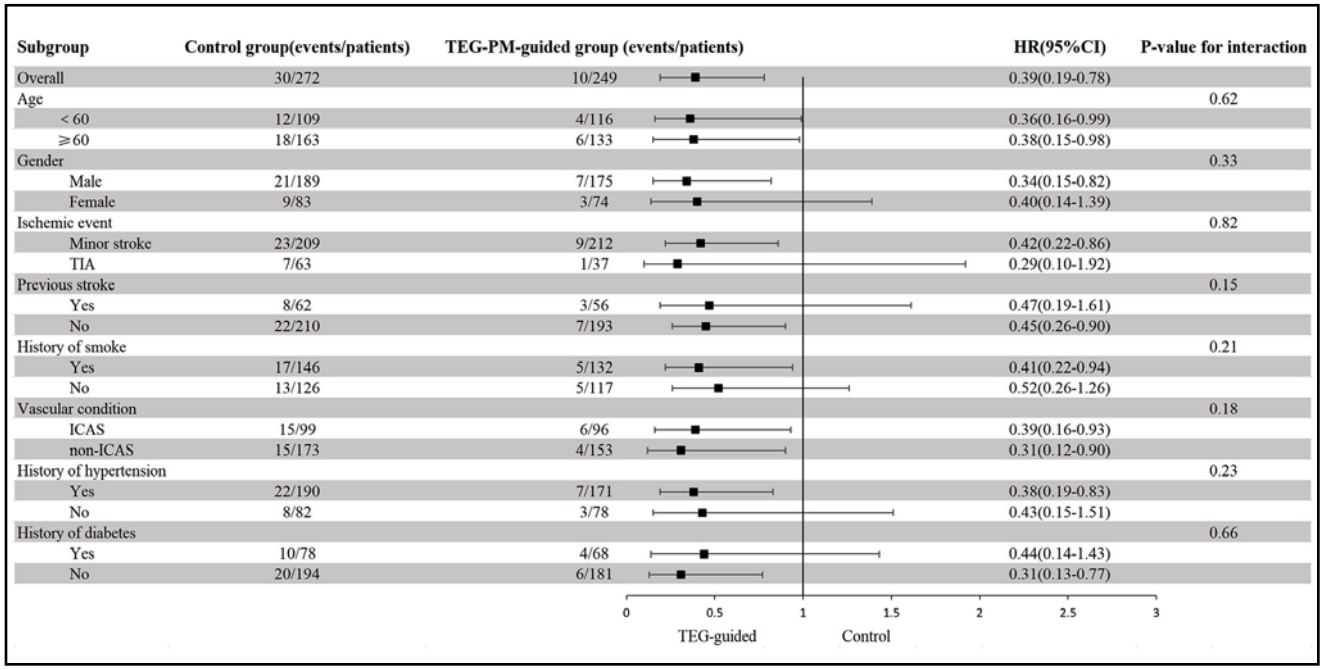

Fig. 1. Hazard ratio for the primary endpoint in prespecified subgroups.

non-TEG-PM-guided subgroup (HR: 0.31; 95% [CI]: 0.12-0.90; $p = 0.02$). Fatal or disabling stroke occurred in 1 patient (0.7%) and 9 patients (5.2%) in the TEG-PM-guided and the control subgroup, respectively ($p = 0.02$) (Table3). There was no statistically significant evidence for the interaction on the effects of TEG-PM guided vs Non-TEG-PM guided on the primary outcome of stroke among patients with and without ICAS (interaction $p = 0.18$; figure 1). There were no significant interactions in any of the prespecified subgroups ($p > 0.1$ for all comparisons).

Secondary efficacy outcomes and Bleeding events

In patients with non-stented ICAS, major vascular events occurred in 6 patients (6.3%) in the TEG-PM-guided subgroup compared with 17 patients (17.2%) in the non-TEG-PM-guided group (HR: 0.37; 95% [CI]: 0.17-0.91; $p = 0.02$). TIA occurred in 2 patients (2.1%) in the TEG-PM-guided group and in 4 (4.0%) in the control group (HR: 0.56; 95% [CI]: 0.14-2.88; $p = 0.71$). Bleeding events occurred in 2 patients (2.1%) in the TEG-PM-guided group and in 3 (3.0%) in the non-TEG-PM-guided group ($p = 0.68$) (Table 3).

For patients without ICAS, major vascular events occurred in 5 patients (3.3%) in the TEG-PM-guided subgroup compared with 16 patients (9.2%) in the non-TEG-PM-guided group (HR: 0.35; 95% [CI]: 0.14-0.95; $p = 0.03$). TIA occurred in 3 patients (2.0%)) in the TEG-PM-guided group and in 6 (3.5%) in the control subgroup ($p = 0.62$). The rate of mild bleeding events, which was defined by the GUSTO criteria, occurred in 2 patients (1.3%)) in the TEG-PM-guided group and in 2 (1.2%) in the non-TEG-PM-guided group ($p = 0.90$) (Table 3).

DISCUSSION

The necessity of drug selection for MAPT after DAPT

DAPT has been demonstrated as a promising approach for patients with TIA or small stroke and several national guidelines recommended a general duration of aspirin plus clopidogrel between 21 days and 90 days (Wang *et al.* 2013; Wang *et al.* 2015). However, after the end of DAPT in these studies, it was often up to the clinician or patient to choose whether to take clopidogrel or aspirin, or neither. In the CHANCE sub-study, as a covariate, the selection of platelet aggregation inhibitors for MAPT had no effect on the net benefit in the DAPT arm within one year (Wang *et al.* 2015). Nevertheless, a certain proportion of patients in the DAPT arm require longer or even lifelong protection of the MAPT for recurrent strokes due to vulnerable intracranial atherosclerotic plaques, insufficient perfusion, and arterial stenosis progression (Li *et al.* 2017). Consequently, clinicians accustomed to randomized drug selection of MAPT after DAPT may expose their patients to inadequate protection against platelet aggregation, putting them at serious risk of stroke. Therefore, the question of whether drug screening increases the net benefit of MAPT after DAPT remains to be investigated.

According to the previous DAPT trials, the risk of stroke recurrence gradually decreased within the first three weeks after a minor ischemic stroke or TIA (Pan *et al.* 2017). But even after this high-risk period treated with DAPT, this decrease in risk does not mean that new ischemic events will not return. Our results showed that even after DAPT, 30 patients (11.0%) in the non-TEG-PM-guided group experienced a recurrence

Tab. 3. Efficacy and Safety Outcomes

Outcomes	ICAS				Non-ICAS			
	TEG-PM-guided	Non-TEG-PM-guided	HR (95% CI)	*p*-value	TEG-PM-guided	Non-TEG-PM-guided	HR (95% CI)	*p*-value
Efficacy outcomes								
Primary efficacy outcome, n (%)								
Stroke	6 (6.3)	15 (15.2)	0.39 (0.16-0.93)	0.03	4 (2.6)	15 (8.7)	0.31 (0.12-0.90)	0.02
Secondary efficacy outcomes, n (%)								
Ischemic stroke	6 (6.3)	15 (15.2)	0.39 (0.16-0.93)	0.03	4 (2.6)	15 (8.7)	0.31 (0.12-0.90)	0.02
Hemorrhagic stroke	1 (1.0)	2 (2.0)	0.60 (0.14-1.94)	0.58	0 (0)	2 (1.2)	0.94 (0.92-0.95)	0.99
TIA	2 (2.1)	4 (4.0)	0.56 (0.14-2.88)	0.71	3 (2.0)	6 (3.5)	0.65 (0.23-2.36)	0.62
Myocardial infarction	0 (0)	2 (2.0)	0.99 (0.96-1.02)	0.50	1 (0.7)	2 (1.2)	0.57 (0.06-1.05)	0.64
Vascular death	0 (0)	1 (1.0)	1.06 (1.04-1.08)	0.99	0 (0)	0 (0)	NA	NA
Death from any cause	2 (2.1)	1 (1.0)	2.14 (0.24-2.39)	0.54	1 (0.7)	2 (1.2)	0.57 (0.06-1.05)	0.64
*Composites of major vascular events	6 (6.3)	17 (17.2)	0.37 (0.17-0.91)	0.02	5 (3.3)	16 (9.2)	0.35 (0.14-0.95)	0.03
Safety outcomes, n (%)								
Moderate-to-severe bleeding	0 (0)	1 (1.0)	1.05 (1.03-1.07)	0.99	0 (0)	1 (0.6)	0.99 (0.98-1.01)	0.99
Mild bleeding	1 (1.0)	3 (3.0)	0.42 (0.11-1.69)	0.64	2 (1.3)	2 (1.2)	1.16 (0.19-2.04)	0.90
Any bleeding	2 (2.1)	3 (3.0)	0.75 (0.18-2.12)	0.68	2 (1.3)	4 (2.3)	0.61 (0.15-1.57)	0.79

NA=Not applicable.
*Composites of major vascular events including stroke, myocardial infarction, or vascular death.

of stroke at a mean follow-up of 18.1 months. In addition, drug screening of MAPT could dramatically reduce stroke recurrence rate by 8.9% in patients with ICAS. This effect may be due to low platelet reactivity (LPR) with aspirin or clopidogrel or both (35.7% overall in the present cohort). Another explanation is that the Asian population in our study is more prone to ICAS and clopidogrel resistance than Caucasians (Kim & Bonovich, 2014). If both conditions are present in one patient, the recurrent stroke risk will be higher than that without this circumstance. Therefore, our findings suggested that a process of drug selection is required for long-term MAPT after DAPT, especially in ICAS patients. Moreover, even a previous study based on an Asian population showed no significant difference in response to DAPT between patients with and without ICAS at 90 days, our results represented a "better once than never" strategy for reducing long-term stroke risk in symptomatic, unstented ICASs (Liu *et al.* 2015).

The feasibility of TEG-PM to guide MAPT secondary to DAPT

As an unnoticed issue, validation of the effectiveness of the MAPT secondary to DAPT was still problematic in clinical practice (Wang *et al.* 2015).() Various methods have been described for assessing platelet inhibition by antiplatelet drugs, including Platelet Function Tests (PFTs) and gene screening. However, the results of genetic tests can only partially explain the insufficient inhibition of platelet aggregation with clopidogrel, and the various evaluations of platelet function inhibited by clopidogrel are even test-specific (Fontana *et al.* 2011; Hochholzer *et al.* 2010; Lewis *et al.* 2020; Shuldiner *et al.* 2009). Compared with the prevalence of aspirin/clopidogrel resistance previously determined by various methods, our results showed a relatively higher clopidogrel resistance rate and a lower aspirin resistance rate. One explanation for the higher rate of clopidogrel resistance is that all patients included in this study were of Asian descent, who may be more resistant to clopidogrel than white patients (Kim & Bonovich, 2014). The TEG-PM was once believed to overestimate the resistance to antiplatelet drugs (Tantry *et al.* 2005). Methodologically, multiple factors can impact the sensitivity and specificity of the TEG-PM, including the test conditions (e.g., requirements for temperature and time), platelet responsiveness of patients, clopidogrel and aspirin resistance, genetic factors (e.g., gene polymorphism), clinical factors (e.g., treatment compliance) (Collyer

et al. 2009; Serebruany & Goto, 2008). Nevertheless, even with deviations, this platelet function test still plays a bigger role than ever in the assessment for antiplatelet medication (Fontana *et al.* 2020). Although the TEG-PM assay does not cover complete validation of platelet function in the present study, it saves at least a certain number of patients from inadequate platelet aggregation inhibition within a relatively long period (mean, 18.1 months). As a tangible platelet function test, TEG-PM may reflect, at least in part, the efficacy of antiplatelet therapy, which may be of clinical benefit, particularly in high-risk patients. Therefore, the use of the TEG-PM can be a suitable aid for determining the treatment and the correct choice of medicine. However, it is still important that the treatment of each patient is individual and is influenced by several factors (race, gender, genetics etc.). Of note, 32.5% (n=81) of our patients did not respond to clopidogrel. In this subset of patients, particularly those with more severe untreated risk factors (e.g. ICAS), the casual use of clopidogrel as a MAPT can be new-stroke-causative even after the acute phase.

Study limitations

(1) This retrospective study was more prone to a certain bias compared with the prospective randomized trial. (2) Our study was conducted based on the demographic characteristics of the Asian population, which has a higher incidence of ICAS and a higher prevalence of genetic polymorphisms affecting clopidogrel metabolism, so the population-specific experience may not be globally generalized. (3) Due to a relatively small sample size of patients with drug resistance, the alternative drug to aspirin or clopidogrel should be further investigated.

CONCLUSIONS

The TEG-PM could be a tangible preprocessing in drug selection for MAPT following DAPT in patients with minor strokes or TIAs, especially for those with non-stented ICASs.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Informed consent form was obtained from each study participant, and the study was approved by the local review board of China and Japan Union Hospital of Jilin University (No.2020-NSFC-087).

AVAILABILITY OF DATA AND MATERIALS

The datasets used and analyzed in the study are not publicly available due potential identifiability but are available from the corresponding author on reasonable request are available from the corresponding author on reasonable request.

COMPETING INTERESTS

The authors declare that they have no competing interests.

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AUTHORS' CONTRIBUTIONS

Lei Yan and Wenzhao Liang: study design, statistical analysis, drafting of manuscript, and manuscript revision. Bingyang Zhao and Zhongyu Zhao: statistical analysis, and significant review of the manuscript. Kai Zhang ang Lingling Wang: study design and manuscript revision. Jing Mang: study design, interpretation of study findings, and significant review of the manuscript. All authors reviewed the manuscript for intellectual content, approved the final version, and agreed to be accountable for the work.

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