Supplemental Methods

Title: Optimal Duration of Dual Antiplatelet Therapy for Minor Stroke Within 72 Hours of Symptom Onset: A Prospective Cohort Study

A. Data collection

The researchers prospectively collected data on demographic, clinical, imaging, and laboratory findings. Baseline data, including NIHSS scores, were collected for all the patients, and the stroke subtypes were classified according to the TOAST criteria after complete diagnostic profiling. The following data were directly obtained from the registry database: (1) demographics, including age, sex, body mass index, smoking, admission systolic blood pressure (SBP), and diastolic blood pressure (DBP); (2) medical history, including previous TIA, previous stroke, previous coronary artery disease (CAD), previous peripheral artery disease (PAD), hypertension (HTN), diabetes mellitus (DM), dyslipidemia, smoking, and atrial fibrillation (AF); (3) previous medication, including previous antiplatelet, anticoagulated, antihypertensive and statins medication use; (4) stroke characteristics, including the time from onset to arrival(categorized as ≤ 24 hours and among 24 hours to 72 hours), initial NIHSS scores (categorized as ≤ 3 score and between 4 to 5 score), pre-stroke mRS score, and ischemic stroke subtype according to the TOAST criteria; (5) laboratory data, including white blood cell counts, creatinine serum levels, platelet counts, international normalized ratio (INR), urea, homocysteine (Hcy), and fasting low-density lipoprotein cholesterol (LDL-C); (6) in-hospital treatment, including antiplatelet, lipid lowing, antidiabetic and antihypertensive therapy, and (7) in-hospital imaging evaluation, including cranial MRI/CT examination and vascular examination (TCD/MRA/CTA/DSA) helped to determine the presence of intracranial cerebral atherosclerosis (ICAS), determined by 50%–99% stenosis of large intracranial arteries according to Warfarin-Aspirin Symptomatic Intracranial Disease (WASID) trial criteria; and (8) monitoring of some indicators, including daily blood pressure and blood glucose monitoring record results. For continuous variables, the missing value data were used by multiple imputations, and the optimal imputation data summarized after 25 interpolations were selected by the system for analysis. The study subjects were divided into two groups for comparison according to the initial antiplatelet regimen: single antiplatelet therapy (SAPT) of aspirin monotherapy (AM) or clopidogrel monotherapy (CM) and dual antiplatelet therapy with clopidogrel and aspirin (DAPT with C plus A).

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B. Outcomes

Vascular events were prospectively observed on day 1, day 10, day 21, and day 90±7 after enrollment after the qualifying event via routine clinic visits or telephone interviews performed by dedicated physicians with a predefined protocol.

Definitions of outcome events used in this cohort	
Efficacy outcomes	
Stroke	Sudden symptoms and signs of focal disturbance of cerebral function associated with cerebral circulation disorders. Etiology would be classified based on the SSS-TOAST standard.
Ischemic stroke	Recurrent ischemic stroke: (1) sudden onset of a new focal neurologic deficit, with clinical or imaging evidence of infarction lasting ≥24 hours and not attributable to a nonischemic cause (i.e., not associated with a brain infection, trauma, tumor, seizure, severe metabolic disease, or degenerative neurologic disease), and (2) a new focal neurologic deficit lasting <24 hours and not attributable to a nonischemic cause but accompanied by neuroimaging evidence of new brain infarction. Imaging indicated that the new infarct should be geographically distinct from the original infarct. Progressive ischemic stroke: rapid worsening of an existing focal neurologic deficit (NIHSS increasing ≥4, excluding hemorrhagic transformation after infarction or symptomatic intracranial hemorrhage) lasting >24 hours and not attributable to a nonischemic cause, accompanied by new ischemic changes from the initial infarct on baseline magnetic resonance imaging or computed tomography of the brain.
TIA	It is defined as experiencing acute transient neurological dysfunction during hospitalization, lasting for no more than 24 hours, with no new ischemic lesions observed on cranial MRI; or being diagnosed based on episodic symptoms during follow-up visits after seeking medical attention.
Symptomatic hemorrhagic stroke	Acute extravasation of blood into the brain parenchyma or subarachnoid space with associated neurological symptoms.
Myocardial infarction	Myocardial infarction was confirmed if one had more than two from below: typical chest pain, Troponin elevation, ECG changes (new ST segment changes, new Q wave, or new left bundle branch block).
Angina attacks	Angina is typical when all diagnostic criteria are satisfied, including substernal chest pain, the induction by exertion or emotional distress, and the remission with rest or nitro derivatives. Conversely, angina is defined as atypical when only 2 of these criteria are fulfilled.
Vascular death	Ischemic vascular death: death due to ischemic stroke, myocardial infarction, sudden cardiac death, arrhythmia,

	pulmonary embolism, bowel or limb infarction, or any death not readily attributable to a non-ischemic cause. Hemorrhagic vascular death: death due to intracranial or systemic hemorrhage.
Safety outcome	
Intracranial hemorrhage	The diagnosis is based on hematoma, or its cerebrum, cerebellum, or brain stem scars, on MRI/CT scans. The lesion distribution must be compatible with the neurological symptoms/signs of the patient. However, this subtype does not include hemorrhagic infarction after embolic cerebral infarction.
Any bleeding event	It includes all the following bleeding events: intracranial hemorrhage, skin bleeding, mucous membrane bleeding, gastrointestinal bleeding, and other organ bleeding.

C. Statistical analysis.

The frequency (percentage) is reported, and the mean ± standard deviation or the median (interquartile interval) is reported. We tested for intergroup differences with the t-test for continuous variables and the $\chi 2$ test or Fisher's exact probability test for categorical variables. Univariate ANOVA was used to compare continuous variables for baseline data, and the Least Significant Difference (LSD) method was used for multicombination comparison. The following parameters had missing data that were substituted by multiple imputation: height and weight (4.3% missing), baseline blood pressure (0.33% missing), LDL cholesterol (3.88% missing), creatinine levels (7.53% missing), homocysteine levels (3.69% missing), INR (8.87% missing), platelet counts (7.93% missing), and white blood cell counts (9.03% missing). We also used restricted cubic splines to express the potentially nonlinear relationship of duration of antiplatelet and the primary outcome. A propensity score was calculated using a multivariable cox regression model including all the unbalanced clinical characteristics between the two groups (with a $p<0.10$). We performed a 1:1 matching using the nearest-neighbor matching method and a caliper width of 0.2 of the propensity score. Propensity scores (PSs) were estimated to predict the individual probability of each exposure (DAPT vs. SAPT) from the covariates measured at baseline and to generate comparable datasets. The imbalance between patients receiving DAPT and SAPT treatments was addressed using the propensity score weighting method. This model included the inverse probability of treatment weighting (IPTW) and standardized mortality ratio weighting (SMRW) to reduce the impact of treatment selection bias and other potential confounding factors. Propensity scores (PSs) were estimated to predict the individual probability of

each exposure (SAPT vs. DAPT) based on baseline covariates and generate a comparable dataset. The score was then used for multivariate analysis in subsequent outcome models. The IPTW method was employed, where the weight for subjects in the DAPT group was 1/PS, and the weight for subjects in the SAPT group was 1/(1-PS). The SMRW method was also used, where the weight for subjects in the DAPT group was 1, and the weight for subjects in the SAPT group was PS/(1-PS). Weighted Cox proportional hazards regression models were used to estimate hazard ratios (HRs) and their 95% confidence intervals (CIs). Subgroups were defined based on previous research findings, including age (<65 years and ≥65 years), gender (male and female), smoking status (non-smoker, former smoker, and current smoker), presence or absence of hypertension, diabetes, dyslipidemia, and ischemic stroke, prior antiplatelet therapy, baseline NIHSS score (0-3 and 4-5), onset-to-hospital time (0-24 hours and 24-72 hours), TOAST classification, presence or absence of intracranial arterial stenosis, similarity to RCT population (NIHSS score ≤3 within 24 hours of onset, NIHSS score 0-5 within 24-72 hours of onset, and NIHSS score between 4-5 within 0-72 hours of onset). Long-term secondary preventive medication was divided into four groups: no drug, aspirin monotherapy (AM), clopidogrel monotherapy (CM), and dual therapy with aspirin and clopidogrel (DAPT).