Unstable Carotid Plaque is Associated With Coagulation Function and Platelet Activity Evaluated by Thrombelastography

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Background: Rupture of unstable carotid plaque and consequently occlusive thrombus formation for the most part cause ischemic cerebral vascular event. Many researchers have been studying on the risk predictors of carotid plaque formation. But the risk factors for unstable carotid plaque have not been researched for so much. In the current study, we aimed to evaluate the association of coagulation function and carotid plaque especially unstable plaque by thrombelastography (TEG). *Methods:* This was a cross-sectional study. Consecutive eligible patients with acute ischemic stroke were included and their TEG data were collected. Carotid plaque was evaluated by carotid ultrasound. Echolucent plaque and heterogeneous echo plaque in ultrasound were classified as unstable carotid plaque. Patients were classified according to being with carotid plaque or unstable plaque for comparison. *Results:* Four hundred and seven patients were enrolled. Compared to those without carotid plaques, patients with carotid plaques had higher ages, higher incidence of hypertension and diabetes mellitus, lower k ($P = .017$) and higher angle ($P = .021$) on TEG. In the comparison between groups with unstable plaque and stable plaque, no significant difference was found in baseline characteristics; higher serum fibrinogen and higher maximum amplitude on TEG were significantly correlated to unstable carotid plaques ($P = .051$, $P = .009$). Multivariate logistic analysis revealed that age, hypertension, and smoking were independent risk factors of carotid plaques formation; higher serum fibrinogen was an independent risk factor of unstable plaques formation. *Conclusions:* This study demonstrates that carotid plaques formation in ischemic stroke patients has a link to abnormal coagulation function, while high platelet activity has an additional contribution to unstable plaque formation.

Key Words: Carotid plaque—maximum amplitude—unstable plaque—ischemic stroke—thrombelastography

Introduction

Rupture of unstable carotid plaque and consequently occlusive thrombus formation for the most part cause ischemic cerebral vascular event.[1] Unstable plaque can be assessed by a simple and clinically applicable carotid ultrasound because it has special echo characteristics. Many researches have indicated that carotid plaque with specific characteristics of echogenicity is associated with an increased risk of cerebrovascular events. Among these studies, Topakian et al[2] categorized the carotid plaques according to the echolucency or echogenicity of plaques and found that higher plaque echolucency was related to higher risk of ipsilateral stroke alone. Plaque rupture has been associated with apoptosis of smooth muscle cells by the macrophages in the plaque.[3] Carotid plaque with

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more neovascularization inside it will have more instability and link to higher risk of stroke.[4] Previous researches have indicated that echolucent plaque and heterogeneous echo plaque in the carotid ultrasonography have statistically significant higher density of neovascularization than it in echogenic plaque or isoechoic plaque.[4,5] So, we classified the echolucent plaques and heterogeneous echo plaques as instable plaques and aimed to find out the risk factors of them. Many well-known traditional risk factors such as age, hypertension (HTN), diabetes, smoking, and high low-density lipoprotein cholesterol levels have been proven to have association with carotid plaques formation.[6] However, only few studies had focus on the risk factors for unstable carotid plaque formation. For example, Sundström et al[7] found that high eosinophil cationic protein (a marker of eosinophil activity and degranulation) is associated with higher prevalence of carotid plaque and increased incidence of ischemic stroke. So how about platelets and coagulation function? Because hypercoagulability is a strong risk factor of thromboembolism,[8] we think abnormal coagulation function may also associate with carotid plaques formation. As to detect coagulation function, a fast and comprehensive method is needed. Thrombelastography (TEG), a fast and efficient test method with high specificity, cannot only exam coagulation and fibrinolysis process, but also be used to detect platelet functions.[9] Maximum amplitude (MA), probably the most important index on TEG, is taken to represent the maximal clot strength.[10] High MA indicates hypercoagulability and can be attributed to high platelet reactivity and generation of thrombin on the surface of activated platelets.[11,12] Therefore, the objective of this research is to find out the association between indexes of TEG and the formation of carotid plaque especially unstable carotid plaque detected by ultrasonography.

Materials and Methods

Study Population

This is a cross-sectional study that enrolled 407 patients with consecutive acute ischemic stroke (AIS) who were receiving treatment in Neurology Department of Renji Hospital between 2013 and 2014. Shanghai Renji Hospital is a major teaching hospital of the Medical School of Shanghai Jiao Tong University. Nearly 60-80 AIS patients were admitted to the department every month. The study included eligible patients at hospital admission and collected TEG data and other baseline data. All patients included in the study would receive routine therapies for ischemic stroke. It is remarkable that antiplatelet and hypolipidemic agents would be given to all patients unless they have contraindications. There are 3 antiplatelets regimes we usually use: (1) aspirin 100-300 mg daily is the first choice; (2) clopidogrel 75 mg daily loaded with a dose of 150-300 mg is the substitution if there is contraindication for aspirin use; (3) dual antiplatelet therapy including aspirin and clopidogrel will be applied if patients have progressive ischemic strokes. Atorvastatin or rosuvastatin was regular hypolipidemic agent we applied.

Patients' exclusion criteria (those meeting one of the following criteria would be excluded): age below 18 years; missing admission TEG; after thrombolysis therapy; history of hematologic diseases; prothrombin time greater than 1.5 times control; platelet count less than 100,000/mm^3; patients taking anticoagulant therapy; patients refusing to participate in the current study or refusing the follow-ups.

The study was approved by the Ethics Committee of Renji Hospital. Informed consent was obtained from all the included patients.

Baseline Data Collection

Many medical history and lab test data were included in baseline data collection: age, gender, HTN (defined as the use of antihypertensive agents or systolic blood pressure ≥140 mm Hg or diastolic blood pressure ≥90 mm Hg), diabetes mellitus (DM; defined as the use of oral hypoglycemic agents, insulin, or a fasting serum glucose level higher than 7.0 mmol/L on at least 2 separate occasions), hyperlipidemia (defined as the use of lipid-lowering agents or a serum total cholesterol level ≥5.7 mmol/L or low-density lipoprotein (LDL) cholesterol level ≥3.4 mmol/L), ischemic heart disease (a history of acute myocardial infarction or angina pectoris), and atrial fibrillation (previously diagnosed by a cardiologist or if the arrhythmia was found on an electrocardiograph (EKG) record performed after admission). Other routine tests after admission included blood cell count, renal and liver function tests, blood glucose, hemoglobin A1c (HbA1c), electrolytes, lipid profile, prothrombin time, international normalized ratio, activated partial thromboplastin time, and fibrinogen.

Thrombelastography Analysis

TEG is a routine examination for stroke inpatients admitted to the Neurology Department of our institute. Blood samples for the test of TEG were obtained at least 3 days after the application of antiplatelet agents when these agents had reached the steady blood concentrations. Whole blood was collected in a 3.2% sodium citrate Vacutainer tube (BD, Franklin Lakes, New Jersey) and TEG was performed within 90 minutes after collection using a computerized TEG coagulation analyzer according to the manufacturer's instructions (TEG model 5000, Haemoscope Corporation, Niles, IL). Citrate plasma was mixed with kaolin, inverted 5 times, and then loaded in a heparinase-coated cup. Thrombelastography was stopped after maximal fibrin clot strength was recorded. Many major components in TEG had been recorded: (1) the reaction time (r) indicates the recalcification and drawing of the plasma and activity of clotting factors. (2)The coagulation time (k) indicates the clot formation time and activity

of fibrous protein (same as the angle). (3) The MA of the graph represents the maximal elasticity of the clot and activity of platelet.[13]

Carotid Plaque Ultrasound Assessment

Carotid plaques were assessed in the supine position using B mode ultrasonography (MACROMAXIII, Sonosite) with a 4- to 10-MHz linear array transducer. Extracranial carotid artery trees (common carotid artery, the bifurcation, internal and external carotid artery) on both sides were screened for plaque. Images were obtained and digitally stored according to a standard protocol. Both longitudinal and transvers dynamic images of each plaque were stored.[14] Plaques are defined as focal structures that encroach into the arterial lumen by at least .5 mm or 50% of the surrounding intima-media thickness or demonstrate a thickness of >1.5 mm, as measured from the intima-lumen interface to the media adventitia interface.[15] Subjects with carotid plaque were definite as present of ≥1 lesions, no matter the numbers of carotid plaque. Carotid plaques were classified into 4 types according to the characteristics of their echogenicity: type 1, echogenic (higher content of fibrous tissue and calcification); type 2, echolucent (lipid rich); type 3, heterogeneous (mixed echolucent and echogenic); and type 4, isoechoic (homogeneous echogenicity similar to muscular tissue).[2] Patients with echolucent or heterogeneous types of plaque were categorized as unstable plaque group, while patients with echogenic or isoechoic type of plaque but without types 2 and 3 plaque were categorized as stable plaque group.

Statistical Analysis

We adopted statistical software SPSS 17.0 to conduct data analysis in this research. Student's t test or Mann-Whitney Utest was adopted for the continuous variable comparison between groups, while chi-square test or Fisher's exact test was adopted for categorical variable comparison. Taking $P<.05$ as data has a significant difference. All variables with a $P < .1$ on univariate analysis were entered into stepwise logistic regression analysis.

Result

Of the 407 individuals, whose mean age is 65.6 years, 278 are male (68.3%). According to the measurement of carotid artery ultrasound, carotid plaque was found in 64.7% of patients, and 53.8% for echolucent plaques, 47.7% for isoechoic plaques, 36.6% for echogenic plaques, and 24.0% of heterogeneous echo plaques.

Table 1. *Baseline characteristics and admission thrombelastography (TEG) associated with carotid plaques*

	Patients with carotid plaques (n = 263)	Patients without carotid plaques (n = 144)	*P* value
Age (yr)	68.3 (42-94)	60.6 (31-82)	<.001
Male	69.4%	77.9%	.455
Current smoker	45.0%	41.2%	.104
Hypertension	81.8%	63.1%	.003
Diabetes mellitus	43.5%	26.3%	.021
Hyperlipidemia	41.6%	36.8%	.293
Atrial fibrillation	4.3%	2.6%	.857
Ischemic heart disease	7.7%	4.4%	.255
Ischemic stroke or TIA history	33.0%	26.3%	.075
SCr (μmol/L)	78.5 (41-194)	72.6 (39.7-114.8)	.02
HbA1c (%)	6.9 (4-15.4)	6.2 (4.5-12.7)	.001
Triglyceride (mmol/L)	1.45 (.52-4.12)	1.44 (.38-3.35)	.415
Cholesterol (mmol/L)			
LDL (mmol/L)	4.38 (2.22-8.46)	4.33 (2.14-9.21)	.842
Lipoprotein a (nmol/L)	2.62 (.92-6.06)	2.55 (.96-6.62)	.396
aPTT (s)	305.2 (3-2930)	278.6 (1.14-1052)	.293
INR			
TEG-R	28.2 (16.5-53.3)	28.4 (17.9-56.2)	.437
	.93 (.78-1.19)	.92 (.79-1.09)	.173
	6.1 (3.5-8.9)	6.2 (3.3-9.8)	.353
TEG-k (min)	1.9 (.9-18.2)	2.1 (1.0-16.5)	.017
TEG-Angle (deg)	71.0 (54.7-79.7)	69.8 (59.3-78.3)	.021
TEG-MA (mm)	63.6 (20.3-79.2)	62.8 (20.2-76.7)	.437
Fibrinogen (g/L)	3.08 (1.74-6.79)	2.92 (1.39-6.36)	.09

Abbreviations: aPTT, activated partial thromboplastin time; INR, international normalized ratio; SCr, serum creatinine.
Results are expressed as percentage or means with minimum to maximum numbers in parentheses.

Comparison Between Patients With Carotid Plaque and Those Without

Table 1 presents baseline demographics, clinical characteristics, and TEG outcome of patients with carotid plaques and those without. Compared to those without carotid plaques, patients with carotid plaques have higher ages ($P <$ .001), higher incidence of HTN and DM ($P = .003$, $P = .021$), higher SCr and HbA1c ($P = .02$, $P = .001$). Carotid plaque is not correlated to activated partial thromboplastin time and international normalized ratio, but significantly correlated to lower k ($P = .017$), higher angle ($P = .021$) in TEG, which indicates that individuals with carotid plaques have relative fibrous protein hyperfunction.

Comparison Between Unstable Plaque Group and Stable Plaque Group

We define echolucent carotid plaque and heterogeneous echo plaque as unstable plaque, while the other kinds of plaque are defined as stable plaque. So as Table 2 presents, comparison of baseline data and TEG data between patients with unstable plaques and patients only with stable plaques showed that no significant difference is found in baseline characteristics; fibrinogen concentration is associated with unstable plaques ($P = .051$); however, only MA in TEG is significantly correlated to unstable carotid plaques ($P = .009$), which indicated that among the patients with carotid plaques, those who have fibrous protein hyperfunction and platelet hyperfunction are more likely to be burdened with unstable type of carotid plaques.

As Table 3 shows, for confirming the conclusion above, we also compared TEG data of patients with echolucent carotid plaques and heterogeneous echo plaque carotid plaques, respectively, with stable plaque group. The outcome shown that TEG-MA is associated with both echolucent carotid plaque and heterogeneous echo plaque ($P = .015$, $P = .001$). Besides, heterogeneous echo plaque is correlated to k, angle in TEG and fibrinogen ($P = .004$, $P = .039$, $P = .006$).

Outcome of Stepwise Logistic Regression Analysis

All variables with a $P <$ .10 on univariate analysis were entered into stepwise logistic regression analysis: age, smoker, HTN, DM, ischemic stroke or TIA history, serum creatinine, HbA1c, TEG-k, TEG-Angle, fibrinogen concentration for carotid plaques; TEG-Angle, TEG-MA, fibrinogen concentration for unstable plaques; HbA1c ($P = .095$), serum LDL concentration ($P = .074$), atrial fibrillation history ($P = .012$), TEG-k, TEG-Angle, TEG-MA, fibrinogen concentration for heterogeneous echo

Table 2. *Baseline characteristics and admission thrombelastography (TEG) associated with unstable carotid plaques*

	Unstable plaque group (n = 146)	Stable plaque group (n = 63)	*P* value
Age (yr)	67.7 (42-90)	69.7 (46-94)	.225
Male	69.9%	68.3%	.386
Current smoker	47.3%	39.7%	.112
Hypertension	82.9%	79.4%	.486
Diabetes mellitus	45.2%	39.7%	.425
Hyperlipidemia	40.4%	44.4%	.455
Atrial fibrillation	5.5%	1.6%	.160
Ischemic heart disease	8.9%	4.8%	.310
Ischemic stroke or TIA history	32.8%	33.3%	.676
SCr (umol/L)	78.5 (41-194)	78.3 (42-159)	.547
HbA1c (%)	6.96 (4.9-15.4)	6.71 (4.0-11.2)	.162
Triglyceride (mmol/L)	1.42 (.57-3.80)	1.53 (.52-4.12)	.485
Cholesterol (mmol/L)			
LDL (mmol/L)	4.40 (2.5-8.46)	4.34 (2.22-6.79)	.245
Lipoprotein a (nmol/L)	2.65 (1.13-6.06)	2.57 (.92-4.29)	.477
aPTT (s)	287.6 (20-1922)	346.1 (3-2930)	.356
INR			
TEG-R	28.3 (16.5-53.3)	28.0 (17.8-35.7)	.794
	.93 (.79-1.10)	.92 (.78-1.19)	.975
	6.09 (3.5-8.9)	6.07 (3.8-8.6)	.662
TEG-k (min)	1.9 (.9-14.9)	2.1 (.9-18.2)	.129
TEG-Angle (deg)	71.3 (54.7-79.6)	70.1 (57.5-79.7)	.08
TEG-MA (mm)	64.1 (20.3-79.2)	62.4 (20.3-76.2)	.009
Fibrinogen (g/L)	3.16 (1.84-6.79)	2.88 (1.74-4.84)	.051

Abbreviations: aPTT, activated partial thromboplastin time; INR, international normalized ratio.

Results are expressed as percentage or means with minimum to maximum numbers in parentheses. *Unstable plaque group* represents the patients with echolucent carotid plaques or heterogeneous echo plaque; *stable plaque group* represents patients with echogenic or isoechoic type of plaque but without unstable type (types 2 and 3) of plaque.

Table 3. *Comparison of admission thrombelastography (TEG) associated with echolucent carotid plaques and heterogeneous echo plaque carotid plaques to stable plaques*

	Echolucent carotid plaques (n = 116)	*P* value*	Heterogeneous echo plaques (n = 53)	*P* value†
TEG-R	6.14 (3.5-8.5)	.662	6.03 (3.8-8.9)	.723
TEG-k (min)	1.84 (.9-9.2)	.271	1.78 (1.0-14.9)	.004
TEG-Angle (deg)	71.1 (54.7-79.6)	.180	72.7 (61.8-79.1)	.039
TEG-MA (mm)	63.8 (20.3-79.2)	.015	66.5 (20.7-79.0)	.001
Fibrinogen (g/L)	3.09 (1.84-6.54)	.113	3.33 (2.06-6.79)	.006

Results are expressed as means with minimum to maximum numbers in parentheses.
*P value: stable plaque versus echolucent carotid plaques.
†P value: stable plaque versus heterogeneous echo plaques.

Table 4. *Evaluation of independent predictors of carotid plaques formation, unstable plaques, heterogeneous echo plaques, and hypoecho plaques by stepwise logistic regression analysis*

	Risk factors	*P* value	OR	95% CI of OR
Carotid plaques	Age	<.001	1.066	1.040-1.093
	Hypertension	.025	1.959	1.108-3.463
	HbA1c	.02	1.278	1.096-1.491
Unstable plaques	Smoking	.025	1.820	1.077-3.074
	Fibrinogen	.018	1.743	1.099-2.762
Heterogeneous echo plaques	TEG-Angle	.034	1.121	1.009-1.247
	Fibrinogen	.021	2.169	1.125-4.181
	AF	.024	13.14	1.41-122.7
Echolucent plaques	Age	.008	.961	.933-.989
	Fibrinogen	.042	1.675	1.019-2.754

Abbreviations: CI, confidence interval; OR, odds ratio.

plaques; age (P = .016), smoker (P = .092), TEG-MA, fibrinogen concentration for echolucent plaques.

Significant independent risk factors are shown in Table 4. Using multifactor logistic regression, we came to the outcome: age, HTN, higher HbA1c, and smoking are independent risk factors of carotid plaques formation (P<.001, P = .025, P = .02, P = .025); higher fibrinogen concentration is an independent risk factor of unstable plaques formation (P = .018); TEG-Angle, fibrinogen level, and atrial fibrillation history are independent risk factors of heterogeneous echo plaques formation (P = .034, P = .021, and P = .024). Age and fibrinogen level are independent risk factors of echolucent plaques formation (P = .008, P = .042).

Discussion

Many animal researches or tests in vitro have shown that activation of both platelets and blood coagulation is associated with atherosclerosis, which may cause thrombotic complications.[16-23] In this study, we found that patients with carotid plaques performed significantly different on TEG compared to those without. These data extend our knowledge of different blood coagulation state having impacts on artery plaques in human body. Prandoni et al[8] found that the incidence of carotid plaques was significantly higher in patients with spontaneous venous thrombosis compared to those without, which indicated atherosclerosis may induce venous thrombosis, or the 2 conditions may share common risk factors. At the same time, it can indirectly confirm the association between coagulation function and atherosclerosis. Furthermore, we found that patients with unstable carotid plaques have higher TEG-MA compared to those with stable type of plaques. The maximal amplitude (MA) of the TEG graph represents the maximal elasticity of the clot and activity of platelet,[13] about which no significant difference was found in the comparison between patients with carotid plaques and those without carotid plaques. So this finding indicates that platelet hyperfunction probably is an additional predictor to unstable carotid plaques formation. For further proving this conclusion, TEG of patient with heterogeneous echo plaques and echolucent plaques are compared, respectively, to those with stable type of carotid plaques. The outcome showed that both of these 2 groups with 2 types of unstable carotid plaques have significantly higher TEG-MA than those without unstable types of carotid plaques. At the initial phase of clot formation, platelets adhere to the endothelium coinciding with releasing inflammatory factors and plaque invasion by leukocytes.[16] Massberg et al blockaded platelet adhesion in mice and found which profoundly reduced leukocyte accumulation in the arterial intima and atherosclerotic lesion formation in the carotid artery. Therefore, platelet adhesion was proven to play a critical role in the initiation

Table 5. *Cross-tab of antiplatelet agents and carotid plaques*

Antiplatelet agents	Plaque	No plaque	Total	Ratio of plaque suffering
Aspirin	114	57	169	.67
Clopidogrel	44	15	59	.75
Cilostazol	1	2	3	.33
Dual antiplatelet therapy	105	69	174	.60
Never use any antiplatelet agents	1	1	2	.50
Total	263	144	407	.65
				$P = .229$

of atherosclerosis.[16] Moriwaki et al evaluated 60 patients with risk factors for atherosclerosis by using indium 111 platelet scintigraphy (to detect platelet accumulation) and high-resolution B-mode ultrasonography (to evaluate plaques). The result showed that significantly more platelet accumulation was found in lesions with ulceration and heterogeneous plaque and in those with higher plaque score that represent the risk of causing vascular occlusion.[24] Here for the first time using TEG to evaluate coagulation function and platelet activity, we show that abnormal coagulation function is an important risk factor for carotid plaque formation while too active platelets will probably increase instability of plaques. Our study proved that antiplatelet drugs are important in antiatherosclerotic therapies.

Other well-known traditional risk factors such as age, gender, history of HTN or DM, smoking, and hyperlipidemia are also evaluated in this study. Age is an independent but unmodifiable risk factor for all kinds of carotid plaque. HTN and DM are both independent risk factors for atherosclerosis, which points to importance of controlling high blood pressure and HbA1c for prevention from artery plaques. As to smoking, it is interesting that not very significant difference about smoking history was found between subjects with carotid plaques and those without but the outcome of multifactor logistic regression indicated that smoking was an independent risk factor for atherosclerosis. Therefore, smoking would indeed do harm to arterial vascular wall. Lianduo[25] did a community-based study to research the risk factors of plaque burden who used the same method with us to classify carotid plaques according to echogenicity on ultrasound images, and his study had proved that traditional risk factors including aging, HTN, and current smoking were associated with carotid plaque burden.

Although, we for the first time came to the association between coagulation function and carotid plaques using TEG to evaluate it, there are still limitations with regard to participant follow-up and ultrasound technology and single-center study. Limited by human resources and time, we did not follow up any recurrence of cerebral vascular events, so this study did not show that abnormal coagulation function is predictive for stroke patients' prognosis. But many studies had confirmed the association between carotid plaque burden together with its echo feature and major atherosclerotic vascular event.[4,26] Ultrasound technology has many advantages like low cost, high efficiency, and capacity to evaluate internal characteristics of plaques. However, it is not the most accurate test to estimate carotid stenosis. So our study does not establish a causative role of abnormal coagulation function in atherosclerosis, but it provides a new evidence from quantification by TEG that abnormal coagulation and platelet functions contribute significantly to carotid plaques especially unstable plaques formation risk. At last, influence of medicine should be taken into consideration. Intake of antiplatelets agents might influence TEG test performance. Hypolipidemic such as statins might exacerbate plaques' unstableness. However, according to the guidelines for the hospital management of AIS patients made by institutes of Europe and the USA, administration of antiplatelet agents is strongly recommended in patients with AIS within 24-48 hours after onset and in-hospital management (level A of evidence); high-intensity statin therapy is strongly recommended to be initiated or continued as first-line therapy in women and men ≤75 years of age who have clinical arteriosclerotic cardiovascular disease, unless contraindicated (level A of evidence).[27,28] So, it is against ethics if we did not give antiplatelet agents and statins for the patients with AIS in our hospital. For the best effect of recover and prevention of recurrence, we gave all patients antiplatelets and hypolipidemic agents by routine. However, we believed that bias caused by antiplatelet and statin application in comparison of TEG results has been reduced to be very small. We aimed to prove that abnormal function of coagulation and platelets will contribute to higher severity of unstable carotid plaques. Of the 407 patients, 405 patients had used antiplatelets and 404 patients had taken statins, so the intake of those medicines would make an effect to the same direction on the TEG and

Table 6. *Kruskal-Wallis test of the TEG and antiplatelet agents*

	TEG-R	TEG-K	TEG-Angle	TEG-MA
P value	.148	.099	.516	.697

Table 7. *Cross-tab of statins and carotid plaques*

Type of statins	Plaque	No plaque	Total	Ratio of plaque suffering
Atorvastatin	149	70	219	.68
Rosuvastatin	109	73	182	.60
Dual statins therapy	3	0	3	1
Never use any statins	2	1	3	.67
Total	263	144	407	.65
				$P = .208$

Table 8. *Kruskal-Wallis test of the TEG and statins*

	TEG-R	TEG-K	TEG-Angle	TEG-MA
P value	.620	.479	.742	.980

plaques instability. In addition, blood samples for the test of TEG were obtained at least 3 days after the application of antiplatelet agents when these agents had reached the steady blood concentrations. Otherwise, we compared the TEG outcomes and carotid plaque burden between patients administrated different antiplatelets regimens. As shown in Tables 5 and 6, using chi-square test for carotid plaque burden and Kruskal-Wallis test for TEG outcome, we came to the conclusion that there is no significant difference in the TEG outcome the ratio of plaque suffering between patients using each antiplatelet agent. Similarly, as Tables 7 and 8 show, no significant difference of carotid plaque burden and TEG was found in patients taking different kinds of statins.

Conclusion

Carotid plaque formation is associated with too fast clot formation and higher activity of fibrous protein. Besides, some traditional risk factors like age, HTN, DM, and smoking are also confirmed being independent risk factors for plaques formation in this study. Furthermore, higher activity of both fibrinogen and platelets is associated with an unstable type of plaques (both heterogeneous echo carotid plaque and echolucent plaque). In conclusion, this study demonstrates that carotid plaques formation in ischemic stroke patients has a link to abnormal coagulation function, while high platelet activity has an additional contribution to unstable plaque formation.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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