Ticagrelor versus Clopidogrel in the Dual Antiplatelet Regimen for Intracranial Stenting or Flow-Diverter Treatment for Unruptured Cerebral Aneurysms: A Single-Center Cohort Study

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ABSTRACT

BACKGROUND AND PURPOSE: Ticagrelor is a novel P2Y12 antagonist, and little is known about its efficacy and safety in the endovascular treatment of aneurysms. This study evaluated the efficacy and safety of ticagrelor versus clopidogrel for stent-assisted coiling or flow-diversion treatment in patients with unruptured cerebral aneurysms.

MATERIALS AND METHODS: From November 2003 to February 2019, two hundred one patients (mean age, 57.5 years; 156 women) with 233 unruptured aneurysms underwent stent-assisted coiling or flow-diversion treatment. All patients received antiplatelet therapy of aspirin plus clopidogrel (clopidogrel group, 121 patients with 140 aneurysms) or aspirin plus ticagrelor (ticagrelor group, 80 patients with 93 aneurysms). The clinical and radiologic data in each group were retrospectively reviewed and compared.

RESULTS: Two hundred thirty-six procedures were performed, including stent-assisted coiling ($n = 101$) and flow diversion ($n = 135$). At 90 days, the primary outcome—a composite of any stroke and death—occurred in 9.9% of the clopidogrel group and 8.6% of the ticagrelor group ($P = .822$). Ischemic stroke occurred in 10 (7.0%) of the clopidogrel group and 7 (7.5%) of the ticagrelor group ($P > .999$). Disabling stroke occurred in 4 (2.8%) in the clopidogrel group and in 4 (4.3%) in the ticagrelor group ($P = .716$). Ninety-day death occurred in 3 (2.1%) in the clopidogrel group and 1 (1.1%) in the ticagrelor group ($P > .999$). Any bleeding at 90 days occurred in 13 (9.2%) in the clopidogrel group and 6 (6.5%) in the ticagrelor group ($P = .479$).

CONCLUSIONS: Ticagrelor appears to be as effective and safe as clopidogrel in stent-assisted coiling or flow-diversion treatment for unruptured cerebral aneurysms.

ABBREVIATION: DAPT = dual antiplatelet therapy

Endovascular coiling is an established treatment for ruptured or unruptured cerebral aneurysms.[1,2] However, some aneurysms, such as wide-neck, large, or giant and dissecting fusiform aneurysms, are still challenging. Currently, stent-assisted coiling and flow diversion have been widely accepted as potential treatment modalities for challenging or uncoilable lesions. However, thromboembolic complications are still a risk in stent-assisted coiling and flow-diversion procedures.

Dual antiplatelet therapy (DAPT) with aspirin plus clopidogrel is a first-line regimen for neuroendovascular procedures.[3,4] However, individual responses to clopidogrel are varied,[5] and hyporesponse is commonly reported.[6] Unfortunately, hyporesponse to clopidogrel increases the risk of thromboembolic events.[7-9] Thus, to minimize any complications related to procedures or DAPT, novel antiplatelet medication may be of benefit for patients undergoing neuroendovascular procedures.[10,11]

Ticagrelor is an oral and reversible P2Y12 antagonist approved by the FDA in 2011.[12] Large trials have proved the efficacy and safety of ticagrelor for coronary disease.[13,14] Because of its success with coronary disease, ticagrelor treatment has also been attempted for cerebrovascular disease[15,16] and was shown to be superior to aspirin in the secondary prevention of stroke under specific circumstances.[17,18] Thus, ticagrelor is emerging as a novel medication for neuroendovascular procedures. However, little is

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known about the efficacy and safety of ticagrelor for the endovascular treatment of aneurysms.

In the present study, the efficacy and safety of ticagrelor treatment in conjunction with stent-assisted coiling or flow-diversion treatment in patients with unruptured cerebral aneurysms were evaluated and compared with those of clopidogrel.

MATERIALS AND METHODS

Study Design

University Health Network, Toronto Western Hospital institutional review board approved this study and waived the need to obtain patient informed consent because of the retrospective study design. The study was performed under the guidelines outlined by the Declaration of Helsinki and followed the Strengthening The Reporting of OBservational Studies in Epidemiology (STROBE) checklist (https://www.elsevier.com/__data/promis_misc/ISSM_STROBE_Checklist.pdf).

Participants

From November 2003 to February 2019, two hundred seventy-four consecutive patients underwent stent-assisted coiling or flow diversion for cerebral aneurysms at our institution. Patients treated with DAPT of aspirin plus clopidogrel or ticagrelor were included. Patients treated for ruptured aneurysms, intracranial atherosclerotic stenosis, iatrogenic dissection, or carotid cavernous fistula were excluded. A total of 201 patients with 233 unruptured aneurysms were included and divided into the clopidogrel or ticagrelor group.

Using the electronic patient records and imaging data base, we retrospectively evaluated the characteristics of patients and target aneurysms, procedural details, and clinical and angiographic follow-up results.

DAPT Protocol

Before the procedure, DAPT was administered to patients for at least 3 days according to the institution's protocol.[19] For the clopidogrel group, aspirin (81 mg once daily) and clopidogrel (75 mg once daily) were administered. For the ticagrelor group (due to the change of the operator's preference since 2016), aspirin (81 mg once daily) and ticagrelor (90 mg twice daily) were administered. For patients without any DAPT premedication, a loading dose of aspirin (325 mg) plus clopidogrel (300 mg) or ticagrelor (180 mg) was also administered on the day of the procedure. Neither a platelet function test nor a modification of DAPT was performed.

Under general anesthesia and systemic heparinization, patients underwent stent-assisted coiling or a flow-diversion procedure in the usual manner. Systematic heparinization was performed according to institutional protocol (500-1000 IU/10 kg of body weight of heparin IV following placement of the femoral/radial sheath, followed by a 1000 IU hourly during the procedure). After the procedure, DAPT was maintained for 3–6 months, followed by discontinuation of clopidogrel or ticagrelor treatment. Aspirin monotherapy was maintained indefinitely.

Outcome Measurements

The primary outcome was a composite occurrence of stroke and death within 90 days after the procedure. Stroke was defined as neurologic functional loss by an ischemic or hemorrhagic event, with residual symptoms lasting at least 24 hours or leading to death.[13] The first secondary outcome was a 90-day occurrence of ischemic stroke restricted to the treated vascular territory, identified on CT or MR images. Other secondary outcomes included the following: 1) 90-day occurrence of disabling stroke, which was defined as any ischemic or hemorrhagic stroke with a change of the mRS score of >1,[15] and 2) any death. Additionally, the safety outcome was evaluated, which was defined as a 90-day occurrence of any bleeding event (neurologic or non-neurologic) requiring a medical intervention. The incidence of medication change due to adverse events was also assessed.

Imaging Follow-up

Contrast-enhanced MR angiography was routinely performed for the evaluation of the posttreatment occlusion grade of aneurysms.[20,21] All MR imaging examinations were performed using a 1.5T or 3T MR imaging scanner using gadolinium contrast injected at a rate of 1.5 mL per second to a total of 15 mL followed immediately by a flush of 30 mL of saline. Further details were described in previous studies.[20,21] In some cases, CT angiography was alternatively performed for the evaluation of aneurysms treated using flow diversion only. The final follow-up angiographic imaging was retrospectively reviewed by 2 independent investigators (a neuroradiologist and a neurointerventionalist). In the event of different diagnoses between the 2 investigators, another neurointerventionalist reviewed the data, and all 3 investigators came to a consensus regarding the results. The aneurysm occlusion grade was assessed by the Raymond-Roy occlusion classification, in which class I is defined as complete occlusion; class II, as neck remnant; and class III, as sac remnant.[22] In-stent stenosis was divided into 2 grades: 1) none, or $<50\%$ and 2) $\geq 50\%$. If a stented vessel could not be evaluated due to a "marker band effect,"[21] the results were marked as "unknown."

Statistical Analysis

Univariate analysis to compare baseline characteristics and outcomes between the 2 groups was performed using the χ^2 test, Fisher exact test, Mann-Whitney U test, and standard t tests. For the evaluation of risk factors associated with thromboembolic or hemorrhagic complications after the procedure, all variables with clinical importance were introduced into a multivariate analysis using the binary logistic regression method. Significance was defined as $P < .05$. Statistical analyses were performed using SPSS Statistics 25.0 for Windows (IBM).

RESULTS

Patients and Aneurysms

A total of 201 patients (mean age, 57.5 years; male/female ratio = 45:156) with 233 unruptured aneurysms (saccular, 222; fusiform, 11) were successfully treated. The clopidogrel group consisted of 121 patients with 140 aneurysms, and the ticagrelor group consisted of 80 patients with 93 aneurysms. Baseline characteristics of the patients were not different between the 2 groups (Online Supplemental Data).

Among 233 aneurysms, the presentation, location, and type of aneurysms were not different between the 2 groups. However,

Table 1: Procedural details

	Overall	Aspirin+Clopidogrel Group	Aspirin+Ticagrelor Group	*P* Value
Procedures	236	143[a]	93[b]	.283
Stent-assisted coiling (%)	101	57 (39.9)	44[b] (47.3)	
Neuroform (Stryker)	6	5	1	
Enterprise (Cordis)	13	13	0	
Solitaire (Medtronic)	1	1	0	
LVIS (MicroVention)	46	27	19	
LEO (Balt)	17	5	12	
Atlas (Stryker)	15	5	10	
Combined	3	1	2	
Flow diverter (%)	135	86[a] (60.1)	49 (52.7)	
Pipeline (Medtronic)	104	69	35	
Silk (Balt)	19	15	4	
Surpass (Stryker)	12	2	10	

[a]Including 1 salvage therapy for poor wall apposition of Surpass.
[b]Including 2 salvage therapies for coil protrusion and Pipeline flow-diverter migration.

Table 2: Treatment outcomes

	Overall	Aspirin+Clopidogrel Group	Aspirin+Ticagrelor Group	*P* Value
Nonavailable data	1	1	0	
Primary outcome (%)	22 (9.4)	14 (9.9)	8 (8.6)	.822
Secondary outcomes (%)				
Ischemic stroke	17 (7.2)	10 (7.0)	7 (7.5)	>.999
Disabling stroke	8 (3.4)	4 (2.8)	4 (4.3)	.716
Any death	4 (1.7)	3 (2.1)[a]	1 (1.1)[b]	>.999
Safety outcome (%)	19 (8.1)	13 (9.2)	6 (6.5)	.479
mRS (%)				.484
0–2	227 (96.6)	136 (95.8)	91 (97.8)	
3–6	8 (3.4)	6 (4.2)	2 (2.2)	
Medication change (%)	12 (5.1)	6 (4.2)	6 (6.5)	.547

[a]Major infarction due to infectious vasculopathy, retroperitoneal bleeding, and liver failure.
[b]Basilar occlusion.

the median aneurysm size was slightly larger in the clopidogrel group than in the ticagrelor group (8.6 versus 7.0 mm, $P = .006$) (Online Supplemental Data).

Endovascular Procedures

The total number of procedures was 236 (stent-assisted coiling, 101; flow diversion, 135). In the clopidogrel group, stent-assisted coiling procedures totaled 57 (39.9%) and flow diversion totaled 86 (60.1%), including 1 salvage treatment for poor wall apposition of a flow-diversion device. In the ticagrelor group, stent-assisted coiling totaled 44 (47.3%), including 2 salvage treatments: 1 for coil protrusion and 1 for flow-diverter migration, and flow diversion totaled 49 (52.7%). Procedure types were similarly distributed between the 2 groups ($P = .283$) (Table 1).

Outcomes

All cases were assessed except 1 (nonavailable medical records after discharge) from the clopidogrel group. The primary outcome occurred in 22 cases (9.4%), which was not significantly different between the 2 groups (clopidogrel group, $n = 14$ [9.9%]; ticagrelor group, $n = 8$ [8.6%]; $P = .822$); 90-day ischemic stroke in the treated vascular territory occurred in 10 (7.0%) in the clopidogrel group and 7 (7.5%) in the ticagrelor group ($P > .999$), and 90-day disabling stroke occurred in 4 (2.8%) in the clopidogrel group and 4 (4.3%) in the ticagrelor group ($P = .716$). Ninety-day death occurred in 3 (2.1%) in the clopidogrel group and 1 (1.1%) in the ticagrelor group ($P > .999$). Each cause of death is explained in Table 2.

Ninety-day bleeding events occurred in 19 cases (8.1%, 4 neurologic and 15 non-neurologic), 13 in the clopidogrel group (9.2%) and 6 in the ticagrelor group (6.5%) ($P = .479$). Of the 4 neurologic complications, 2 were due to intraprocedural rupture, 1 was due to nonaneurysmal subarachnoid hemorrhage (clopidogrel group), and 1 was due to hypertensive intracerebral hemorrhage of the basal ganglia (ticagrelor group). All bleeding events were conservatively treated without any disability. Among the 15 non-neurologic complications, 12 were due to puncture site problems (clopidogrel group, $n = 9$; ticagrelor group, $n = 3$), 2 were due to gastrointestinal hemorrhages (1 in each group), and 1 was due to vaginal hemorrhage (ticagrelor group).

Overall, medication was changed in 12 cases (5.1%), slightly more frequently ($n = 6$, 6.5%) in the ticagrelor group than in the clopidogrel group ($n = 6$, 4.2%) because dyspnea ($n = 3$) was more common in the ticagrelor group. However, this result was not statistically different ($P = .547$) (Table 2). After a medication change, all dyspnea was resolved.

Follow-up Imaging

Follow-up imaging data were available for 211 aneurysms (median, 25.1 months; clopidogrel, $n = 126$; ticagrelor, $n = 85$). The median follow-up period was 37.0 months (range, 25.0–48.75 months) in the clopidogrel group and 13.8 months (range, 7.5–23.1 months) in the ticagrelor group ($P < .001$).

Regarding aneurysm occlusion, class I was noted in 154 cases (73.0%), which was the same between the 2 groups (clopidogrel, $n = 92$, 73.0%; ticagrelor, $n = 62$, 72.9%; $P = .552$). In-stent stenosis could not be assessed in 17 cases (8.1%). None or mild in-stent stenosis (<50%) was identified in 114 (90.5%) in the clopidogrel group and 74 (87.1%) in the ticagrelor group ($P = .603$). Follow-up imaging results are shown in Table 3.

Table 3: Radiologic follow-up results

	Overall	Aspirin+Clopidogrel Group	Aspirin+Ticagrelor Group	*P* Value
Follow-up (%)	211/233 (90.6)	126/140 (90.0)	85/93 (91.4)	
Period (median) (IQR) (mo)	25.1	37.0 (25.0–48.75)	13.8 (7.5–23.1)	<.001
Aneurysm occlusion[a] (%)				.552
I	154 (73.0)	92 (73.0)	62 (72.9)	
II	27 (12.8)	14 (11.1)	13 (15.3)	
III	30 (14.2)	20 (15.9)	10 (11.8)	
In-stent stenosis				.603
<50%	188 (89.1)	114 (90.5)	74 (87.1)	
>50%	6 (2.8)	2 (1.6)	4 (4.7)	
Unknown[b]	17 (8.1)	10 (7.9)	7 (8.2)	
Retreatment	16 (6.8)	10 (7.0)	6 (6.5)	>.999

[a]Raymond-Roy Occlusion Classification.
[b]Stented vessel could not be evaluated due to a marker band effect.

Table 4: Risk factors associated with thromboembolic complications

	Odds Ratio	95% Wald CI	*P* Value
Sex	0.736	0.220–2.467	.620
Age	0.999	0.945–1.056	.972
Hypertension	1.652	0.479–5.703	.427
Smoking	0.881	0.265–2.926	.836
Previous stroke/TIA	2.039	0.493–8.427	.325
Dyslipidemia	1.350	0.409–4.458	.622
Prior antithrombotic usage	0.344	0.108–1.098	.072
Aneurysm presentation			
Unruptured, symptomatic	0.914	0.159–5.265	.920
Recurrent or residual	0.659	0.168–2.581	.550
Aneurysm location (posterior circulation)	0.807	0.168–2.581	.774
Aneurysm morphology (fusiform)	4.878	0.885–26.887	.069
Aneurysm size	1.037	0.955–1.127	.386
Antiplatelet medication (ticagrelor)	1.035	0.348–3.083	.950
Treatment technique (flow-diverter)	1.218	0.317–4.676	.774

Table 5: Risk factors associated with hemorrhagic complications

	Odds Ratio	95% Wald CI	*P* Value
Sex	0.640	0.205–1.994	.441
Age	1.013	0.965–1.063	.613
Hypertension	0.549	0.179–1.679	.293
Smoking	1.138	0.385–3.363	.814
Previous stroke/TIA	0.600	0.129–2.796	.516
Dyslipidemia	0.800	0.233–2.744	.722
Prior antithrombotic usage	0.978	0.244–3.928	.975
Aneurysm presentation			
Unruptured, symptomatic	0.380	0.039–3.726	.406
Recurrent or residual	1.187	0.345–4.081	.786
Aneurysm location (posterior circulation)	1.755	0.525–5.864	.361
Aneurysm morphology (fusiform)	0.592	0.060–5.840	.654
Aneurysm size	0.989	0.904–1.083	.812
Antiplatelet medication (ticagrelor)	0.669	0.230–1.946	.461
Treatment technique (flow-diverter)	0.948	0.297–3.025	.929

Risk Factors Associated with Thromboembolic or Hemorrhagic Complications

On multivariate analysis, prior antithrombotic usage (OR = 0.344; 95% CI, 0.108–1.098; $P = .072$) and fusiform morphology (OR = 4.878; 95% CI, 0.885–26.887; $P = .069$) could be associated with the risk of thromboembolic complications within 90 days but were not statistically significant (Table 4). Any risk factors including ticagrelor medication were not associated with hemorrhagic complications within 90 days (Table 5).

Subgroup Analysis by Treatment Technique

When we compared the difference in outcomes according to each treatment technique, there was no difference in outcomes between the clopidogrel and the ticagrelor groups in the stent-assisted coiling subgroup ($n = 100$, non-available data = 1). This finding was the same for the flow-diversion subgroup ($n = 135$) (Table 6).

DISCUSSION

In the present study of patients who underwent stent-assisted coiling or flow diversion for unruptured cerebral aneurysms, the primary outcome (90-day composite of any stroke and death) and secondary outcomes (90-day ischemic stroke, disabling stroke, or any death) were the same in the ticagrelor and the clopidogrel groups. Moreover, 90-day bleeding events did not differ between the 2 groups.

The combination of aspirin plus clopidogrel has been a standard DAPT for neuroendovascular procedures. Clopidogrel is a prodrug whose active form requires a metabolic pathway and irreversibly inhibits a P2Y12 receptor. This process is complex and influenced by several factors. As a result, hyporesponse to clopidogrel is common with a 5%–44% frequency[6] and is known to be associated with a higher risk of thromboembolic events during neuroendovascular procedures.[7-9] The VerifyNow P2Y12 assay (Accumetrics) is widely used for the evaluation of a platelet response in clinical practice.[23] However, there is no standardized definition or cutoff value regarding clopidogrel responsiveness on the VerifyNow assay.[24-26] As a result, regular evaluation of clopidogrel responsiveness and modification of antiplatelet regimens are still controversial.[27]

Unlike clopidogrel, ticagrelor does not require hepatic metabolization for activation, and it reversibly and directly inhibits the

Table 6: Subgroup analysis by treatment technique

	Overall	Aspirin+Clopidogrel Group	Aspirin+Ticagrelor Group	*P* Value
Nonavailable data	1	1	0	
Stent-assisted coiling (%)	100	56 (56.0)	44[a] (44.0)	
Primary outcome (%)	10 (10.0)	6 (10.7)	4 (9.1)	>.999
Secondary outcomes (%)				
Ischemic stroke	6 (6.0)	3 (5.4)	3 (6.8)	>.999
Disabling stroke	2 (2.0)	1 (1.8)	1 (2.3)	>.999
Any death	2 (2.0)	2 (3.6)	0	.502
Safety outcome (%)	9 (9.0)	7 (12.5)	2 (4.5)	.292
Flow-diverter (%)	135	86[b] (60.6)	49 (52.7)	
Primary outcome (%)	12 (8.9)	8 (9.3)	4 (8.2)	>.999
Secondary outcomes (%)				
Ischemic stroke	11 (8.1)	7 (8.1)	4 (8.2)	>.999
Disabling stroke	6 (4.4)	3 (3.5)	3 (6.1)	.668
Any death	2 (1.5)	1 (1.2)	1 (2.0)	>.999
Safety outcome (%)	10 (7.4)	6 (7.0)	4 (8.2)	>.999

[a]Including 2 salvage therapies for coil protrusion and Pipeline flow-diverter migration.
[b]Including 1 salvage therapy for poor wall apposition of Surpass.

P2Y12 receptor with more rapid and greater platelet inhibition.[28] Furthermore, low platelet response is less common in patients using ticagrelor than in those using clopidogrel.[29] On the basis of these results, recent studies have tried to evaluate the safety and efficacy of ticagrelor as an alternative regimen to clopidogrel for neuroendovascular procedures.

Ticagrelor treatment has been attempted for clopidogrel hyporesponders.[30] In a pilot study by Hanel et al,[31] 18 cases of clopidogrel hyporesponders were treated with ticagrelor, ultimately suggesting the potential of ticagrelor as an alternative antiplatelet regimen. In a multicenter cohort study by Moore et al,[32] ticagrelor was administered for clopidogrel hyporesponders ($n = 50$), and outcomes were retrospectively compared with those of clopidogrel responders ($n = 53$). Consequently, thromboembolic and hemorrhagic complications did not substantially differ between clopidogrel (7.9%) and ticagrelor (4.2%) groups in that study.

To directly compare clopidogrel with ticagrelor, Soize et al[33] conducted a 1:1 matched cohort study with 80 patients undergoing flow-diversion or flow-disrupter procedures. In that study, each procedure was performed without either a platelet function test or a modification of antiplatelet therapy, and treatment outcomes between the clopidogrel and ticagrelor groups were directly compared. Among patients in the clopidogrel group, there could be hyporesponders to clopidogrel that affect the unfavorable results. On the other hand, a larger benefit from ticagrelor was anticipated in the ticagrelor group. Nevertheless, that study showed that both treatments were equally safe, and the number of thromboembolic and hemorrhagic complications did not differ between the 2 groups.[33] Similarly, the present study showed that 90-day ischemic stroke occurrence was not statistically different between the 2 groups (clopidogrel group, 7.0%; ticagrelor group, 7.5%; $P > .999$). However, these results should be interpreted with caution due to the relatively small sample size.

In the present study, the rate of ischemic complications in the ticagrelor group appeared to be higher than the values reported by recent studies (4.2%[32] and 2.5%,[33] respectively). For the precise evaluation of complication rates related to DAPT with aspirin plus ticagrelor, Narata et al[34] conducted a retrospective cohort study with 154 consecutive patients who underwent stent-assisted coiling ($n = 41$) or flow-diversion ($n = 113$) treatment. That study included the largest cohort of ticagrelor use in the neuroendovascular field and showed a 1.9% rate of symptomatic ischemic complications after the procedures. In our opinion, this difference was due to 2 disparities: 1) patients with stroke/TIA, and 2) aneurysm size. The present study included 20.9% of patients with stroke/TIA, which was approximately 8-fold higher than in the general population (2.7%).[35] This may have affected the observed rate of ischemic complications. Furthermore, the aneurysm size (median, 7.95 mm) that was included in the present study was demonstrably larger than that in the studies by Moore et al[32] (median, 6 mm) and Soize et al[33] (mean, 6.5 mm). Aneurysm size is a well-known risk factor of complications.[36] Thus, this size disparity may be related to the difference in the observed rate of ischemic complications in the present study. Nevertheless, in the present study, the overall ischemic stroke rate (7.2%) was similar to that found in meta-analyses of stent-assisted coiling[37] and flow-diversion[38,39] treatment. Overall morbidity (3.4%) and mortality (1.7%) were slightly lower than those reported in previous studies.[32-34]

The major concern regarding ticagrelor treatment is the increased rate of fatal intracranial bleeding.[13] However, Narata et al[34] reported a 3.9% rate of intracranial bleeding after ticagrelor treatment, a rate similar to or lower than that found in recent studies of clopidogrel used in stent-assisted coiling (3.0%)[40] and flow-diversion (10.4%)[41] procedures. In the present study, overall intracranial bleeding was 1.7%, with the clopidogrel group (2.1%) showing more bleeding than the ticagrelor group (1.1%) but without any statistical significance. This result was also similar to that found in recent studies of prasugrel used in stent-assisted coiling (2.0%)[10] or in any neuroendovascular procedures (0.7%).[11] Another concern with ticagrelor treatment is dyspnea. In the Platelet Inhibition and Patient Outcome (PLATO) trial, dyspnea occurred more commonly in the ticagrelor group (0.9%).[13] Narata et al[34] also reported 1 case of dyspnea. Similarly, the present study also included 3 cases of dyspnea (3.2%) in the ticagrelor group, which were resolved after a medication change.

In terms of efficacy, the present study also suggested comparable angiographic results regarding the aneurysm occlusion grade, in-stent stenosis, and retreatment between the 2 groups. However, the follow-up period was significantly shorter in the ticagrelor group than in the clopidogrel group (median, 13.8 versus 37.0 months; $P < .001$). Further long-term follow-up is mandatory.

Our study has several limitations. First, because of the limitations inherent in the retrospective design, a selection bias was inevitable regarding the demographics and percentages observed. To lessen selection bias, we included 201 consecutive patients treated with stent-assisted coiling or flow diversion for unruptured cerebral aneurysms. To the best of our knowledge, this study was performed with the largest sample gathered from a single center. The second limitation is a lack of a platelet function test. As mentioned above, we did not use a platelet function test due to its unestablished role in the clinical field. As a result, we could not obtain any laboratory data about the inhibitory effect of each medication on platelets, and we did not modify any antiplatelet regimen. Nevertheless, this is the largest study to directly compare the efficacy and safety of clopidogrel and ticagrelor in neuroendovascular procedures.

CONCLUSIONS

Ticagrelor appears to be as effective and safe as clopidogrel in stent-assisted coiling or flow-diversion treatment for unruptured cerebral aneurysms. A future randomized controlled trial would be ethically feasible and expected.

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