Changing Paradigms of Periprocedural Antithrombotic Therapy in Neuroendovascular Therapy: Analysis of JR-NET 3

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Abstract

To evaluate the changing paradigms of periprocedural antithrombotic management in neuroendovascular therapy in Japan, we analyzed the details of the current periprocedural antithrombotic therapy and compared it with those of the previous generations. We retrospectively analyzed the data from the Japanese Registry of Neuroendovascular Therapy (JR-NET) 3, a nationwide survey in Japan for neuroendovascular therapy between January 2010 and December 2014. A total of 26,233 patients underwent endovascular treatments to usually perform periprocedural antithrombotic therapy were retrospectively analyzed. We compared the results of JR-NET 3 with those of JR-NET 1 (January 2005 and December 2007) and JR-NET 2 (January 2008–December 2009). Post-procedural anticoagulant therapy was less utilized in JR-NET 3 than in JR-NET 2 (53.9% vs. 60.6%, *P* <0.001). Pre-procedural antiplatelet therapy became more frequent and more intensive with each generation. The frequency of aggressive therapy (dual, and triple or more therapy) was 65.2% in JR-NET 3, which was significantly higher than that of JR-NET 1 and JR-NET 2 (41.5% and 61.2%, respectively, *P* <0.001). However, periprocedural ischemic complications (2.0% vs. 5.8%, *P* <0.001) significantly increased, despite aggressive antiplatelet therapy. Neuroendovascular periprocedural antithrombotic therapy is focused more on antiplatelet therapy than on anticoagulant therapy. Currently, antiplatelet therapy is more frequently used with a larger number of multiple agents, however, periprocedural ischemic complications significantly increased.

Key words: neuroendovascular therapy, antiplatelet, anticoagulant

Introduction

The purpose of periprocedural antithrombotic therapy is to prevent periprocedural thromboembolic and ischemic complications. At the site of flow stagnation caused by balloon occlusion, or in the area between catheters, "red thrombus," containing red blood cells and fibrin, is formed by the activation of the coagulation system. To prevent the formation of "red thrombus", anticoagulants such as heparin must be used for critical management as a part of endovascular therapy. However, anticoagulants are not sufficient to prevent the formation of platelet-rich "white thrombus," which is triggered by stent implantation or intimal injury of the arterial vessel.[1,2] Antiplatelet agents play a crucial role in the prevention of systemic atherothrombotic events or local thrombotic complications related to endovascular foreign body implantation. With the progress of endovascular treatment and development of new devices, periprocedural antiplatelet therapy has been more aggressively used in recent years.

Although perioperative antithrombotic therapy might reduce ischemic complications, there is a potential risk of hemorrhagic complications. Several therapeutic

options for antithrombotic therapy exist; however, the optimal management options in neuroendovascular therapy has not been well established.

To evaluate the current perioperative antithrombotic management modalities and the paradigm change with respect to neuroendovascular therapy, we retrospectively analyzed the information from the Japanese Registry of Neuroendovascular Therapy (JR-NET) 3 and compared the data with the data obtained previously in JR-NET 1 and 2.

Materials and Methods

Study population

JR-NET 1–3 were retrospective surveys of the neuroendovascular therapy performed in Japan between January 2005 and December 2007, January 2008 and December 2009, and January 2010 and December 2014, respectively. A total of 26,233 patients registered in JR-NET 3 who underwent the following treatments to usually perform periprocedural antithrombotic therapy were retrospectively analyzed: aneurysm coiling (n = 5494 for ruptured cases, n = 9127 for unruptured cases); parent artery occlusion for dissecting aneurysm or others (n = 854 for ruptured cases, n = 336 for unruptured cases); and percutaneous transluminal angioplasty (PTA) or stenting for cervical carotid artery (n = 8190) or other extra- (n = 1177)/intra- (n = 1055) cranial arteries. Patients with incomplete medical records were excluded from the analysis (lack of detailed information about antithrombotic agents, n = 127; classification failure, n = 23).

To evaluate the changes in antithrombotic therapy paradigms, these data were compared with the data of previous generations, JR-NET 1 and 2,[3)] and to evaluate the change in the frequency of perioperative complications, the percentage of ischemic/hemorrhagic/groin-site complications was compared between JR-NET 2 and 3. Ischemic and hemorrhagic complications were defined as procedure-related and intracranial complications occurring at around 24 h after each procedure. Severe adverse events were defined as death or severe disability with deterioration of ≥2 points of modified Rankin Scale at 30 days after the procedures.

Statistics

Statistical comparisons were made between three groups, namely, between JR-NET 1, 2, and 3, or between two groups, such as between JR-NET 2 and 3 for post-procedural antithrombotic therapy because detailed data regarding postoperative antithrombotic therapy were lacking in JR-NET 1. Categorical variables were presented as counts and percentages, and analyzed using chi-squared tests.

Multiple comparisons were made if an overall significant difference was detected. All of the statistical analyses were performed using SPSS version 21.0 (SPSS Inc., Chicago, IL, USA).

Results

Details of periprocedural antithrombotic therapy between JR-NET 1, 2, and 3

In aneurysm coiling, we reviewed the periprocedural antithrombotic therapy between JR-NET 1, 2, and 3. Compared with JR-NET 1 and 2, pre-procedural antiplatelet therapy was more frequent and more aggressive conducted in JR-NET 3 for both ruptured (Table 1) and unruptured aneurysms (Table 2), and this tendencies were similar to those in post-procedural antiplatelet therapy. With respect to the details of the antiplatelet agents used for ruptured aneurysms, the most frequently used post-procedural antiplatelet regimen was aspirin; however, the percentage decreased from 31.6% in JR-NET 2 to 20% in JR-NET 3. While aspirin monotherapy decreased, cilostazol monotherapy increased from 7.5% in JR-NET 2 to 15.8% in JR-NET 3. For unruptured aneurysms, the most frequently used pre-procedural antiplatelet regimen changed from aspirin monotherapy (40% in JR-NET 1) to dual therapy with aspirin and clopidogrel (53.0% in JR-NET 3). For post-procedural antiplatelet therapy, the most frequent antiplatelet regimen changed from aspirin-ticlopidine dual therapy (11.3% in JR-NET 1) to aspirin-clopidogrel dual therapy (45.6% in JR-NET 3). On the other hand, post-procedural anticoagulant therapy was less utilized in JR-NET 3 than in JR-NET 2 with respect to both ruptured and unruptured aneurysms.

With regards to PTA or stenting, the frequency of pre-procedural antiplatelet therapy was not significantly different between JR-NET 1, 2, and 3 (Table 3). However, compared with JR-NET 1, the frequency of monotherapy decreased (17.2% vs. 6.6%, 7.7%, respectively), whereas the frequency of dual therapy (70.2% vs. 75.6%, 75.3%, respectively) and triple or more therapy (4.6% vs. 8.9%, 12.5%, respectively) were higher in JR-NET 2 and 3. These scenarios were similar to those in post-procedural antiplatelet therapy. The most frequently used periprocedural antiplatelet regimen was changed from aspirin-ticlopidine dual therapy (44% pre- and 40.9% post-procedurally in JR-NET 1) to aspirin-clopidogrel dual therapy (49.1% pre- and 49.2% post-procedurally in JR-NET 3). Post-procedural anticoagulant therapy were less utilized in JR-NET 3 than in JR-NET 2. Only about half of the patients received postoperative anticoagulant therapy.

Table 1 Antithrombotic therapy in aneurysm coiling/parent artery occlusion (ruptured)

| Variables | Ruptured | | |
| | n (%) | | |
	JR-NET 1	JR-NET 2	JR-NET 3
Total number of patients	n = 2004	n = 3978	n = 6348
Pre-procedural antiplatelet therapy			
Yes	119 (5.9)	532 (13.4)	953 (15)*
Monotherapy	90 (4.5)	384 (9.7)*	478 (7.5)
Aspirin	78 (3.9)	327 (8.2)*	335 (5.3)
Ticlopidine	5 (0.3)	5 (0.1)	4 (0.1)
Cilostazol	1 (0.1)	19 (0.5)	45 (0.7)*
Clopidogrel	0	31 (0.8)	85 (1.3)*
Others	6 (0.3)*	2 (0.1)	9 (0.1)
Dual therapy	27 (1.4)	137 (3.4)	415 (6.5)*
ASA–TCL	14 (0.7)*	9 (0.2)	35 (0.5)
ASA–CLP	4 (0.2)	85 (2.1)	298 (4.7)*
ASA–CSZ	9 (0.5)	36 (0.9)	90 (1.4)*
CSZ–CLP	0	7 (0.2)	19 (0.3)
Others	0	0	3 (0.1)
Triple or more	0	4 (0.1)	60 (0.9)*
None	1624 (81)	3290 (82.7)	5151 (81.1)
Unknown	261 (13)	89 (2.2)	244 (3.8)
Post-procedural antiplatelet therapy			
Yes		2175 (54.7)	3700 (58.3)*
Monotherapy	–	1749 (44)	2861 (45.1)
Aspirin	201 (10)	1259 (31.6)*	1272 (20)
Ticlopidine	16 (0.8)*	16 (0.4)	5 (0.1)
Cilostazol	34 (1.7)	298 (7.5)	1001 (15.8)*
Clopidogrel	1 (0.1)	172 (4.3)	479 (7.5)*
Others	–	4 (0.1)	104 (1.6)
Dual therapy	–	318 (8)	735 (11.6)*
ASA–TCL	28 (1.4)*	26 (0.7)	7 (0.1)
ASA–CLP	32 (1.6)	126 (3.2)	410 (6.5)*
ASA–CSZ	2 (0.1)*	147 (3.7)	219 (3.4)
CSZ–CLP	0	12 (0.3)	86 (1.4)*
Others	–	7 (1.31)	13 (0.2)
Triple or more	–	25 (0.6)	104 (1.6)*
None	–	1574 (39.6)*	2405 (37.9)
Unknown	–	162 (4.1)	243 (3.8)
Post-procedural anticoagulant therapy			
Yes	–	1659 (41.7)	2289 (36.1)*
Heparin	356 (17.8)	477 (12)	522 (8.2)
Argatroban	313 (15.6)	712 (17.9)	788 (12.4)
Others	423 (21.1)	670 (16.9)	1429 (22.5)
None	–	2118 (53.2)	3794 (59.8)*

*Indicates significant difference compared with others. ASA: aspirin, CSZ: cilostazol, TCL: ticlopidine.

Table 2 Antithrombotic therapy in aneurysm coiling/parent artery occlusion (unruptured)

Variables	Unruptured n (%)		
	JR-NET 1	JR-NET 2	JR-NET 3
Total number of patients	*n* = 2211	*n* = 4563	*n* = 9463
Pre-procedural antiplatelet therapy			
Yes	1574 (71.2)	3857 (84.5)	8648 (91.4)*
Monotherapy	1033 (46.7)*	1566 (34.3)	2369 (25)
Aspirin	885 (40)*	1013 (22.2)	1185 (12.5)
Ticlopidine	107 (4.8)*	31 (0.7)	3 (0)
Cilostazol	35 (1.6)	61 (1.3)	91 (1)
Clopidogrel	5 (0.2)*	460 (10.1)	930 (9.8)
Others	1 (0.1)	1 (0)	158 (1.7)
Dual therapy	509 (23)	2128 (46.6)	5748 (60.7)
ASA–TCL	274 (12.4)*	113 (2.5)	35 (0.4)
ASA–CLP	51 (2.3)	1253 (27.5)	5013 (53)*
ASA–CSZ	180 (8.1)	672 (14.7)*	408 (4.3)
CSZ–CLP	0	81 (1.8)	285 (3)*
Others	4 (0.2)	9 (1.7)	16 (0.2)
Triple or more	2 (0.1)	30 (0.7)	531 (5.6)
None	523 (23.7)	536 (11.7)	642 (6.8)
Unknown	114 (5.2)*	80 (2)	173 (1.8)
Post-procedural antiplatelet therapy			
Yes	–	3863 (84.7)	8665 (91.6)
Monotherapy	–	1837 (40.3)	2568 (27.1)
Aspirin	229 (10.4)	1319 (28.9)*	1482 (15.7)
Ticlopidine	57 (2.6)*	35 (0.8)	6 (0.1)
Cilostazol	12 (0.5)	157 (3.4)*	178 (1.9)
Clopidogrel	2 (0.1)	323 (7.1)	758 (8)*
Others	–	3 (0.1)	144 (1.5)
Dual therapy	–	1650 (36.2)	5159 (54.5)
ASA–TCL	250 (11.3)*	105 (2.3)	30 (0.3)
ASA–CLP	253 (11.4)	535 (11.7)	4315 (45.6)*
ASA–CSZ	29 (1.3)	928 (20.3)*	454 (4.8)
CSZ–CLP	1 (0.1)	68 (1.5)	354 (3.7)*
Others	–	14 (2.6)	17 (0.2)
Triple or more	–	236 (5.2)	938 (9.9)
None	–	560 (12.3)	612 (6.5)
Unknown	–	50 (1.1)	186 (1.9)
Post-procedural anticoagulant therapy			
Yes	–	2997 (65.7)	5520 (58.3)
Heparin	808 (36.5)*	1264 (27.7)	1519 (16.1)
Argatroban	658 (29.8)*	1868 (40.9)	3785 (40)
Others	78 (3.5)	189 (4.2)*	672 (7.1)
None	–	1391 (30.4)	3630 (38.4)

*Indicates significant difference compared with others. ASA: aspirin, CSZ: cilostazol, TCL: ticlopidine.

Table 3 Antithrombotic therapy in PTA or stenting

Variables	PTA or stenting		
	n (%)		
	JR-NET 1	JR-NET 2	JR-NET 3
Total number of patients	*n* = 2976	*n* = 6724	*n* = 10,422
Pre-procedural antiplatelet therapy			
Yes	2834 (96.6)	6473 (96.3)	9961 (95.6)
Monotherapy	514 (17.2)*	446 (6.6)	806 (7.7)
Aspirin	281 (9.4)*	169 (2.5)	245 (2.4)
Ticlopidine	133 (4.5)*	34 (0.5)	5 (0)
Cilostazol	71 (2.4)*	65 (1)	114 (1.1)
Clopidogrel	11 (0.4)*	130 (1.9)	211 (2)
Others	21 (0.7)	7 (0.1)	231 (2.2)*
Dual therapy	2090 (70.2)*	5080 (75.6)	7848 (75.3)
ASA–TCL	1308 (44)*	697 (10.4)	154 (1.5)
ASA–CLP	128 (4.3)*	2462 (36.6)	5104 (49.1)
ASA–CSZ	590 (19.8)	1352 (20.1)	1430 (13.7)*
CSZ–CLP	6 (0.2)	505 (7.5)	1120 (11)*
Others	58 (1.9)	83 (1.2)	40 (0.4)*
Triple or more	137 (4.6)	598 (8.9)	1299 (12.5)*
None	116 (3.9)	62 (0.9)*	236 (2.3)
Unknown	26 (0.9)	189 (2.8)*	225 (2.2)
Post-procedural antiplatelet therapy			
Yes	–	6519 (97)	10062 (96.5)
Monotherapy	–	382 (5.7)	721 (6.9)*
Aspirin	48 (1.6)	170 (2.5)*	219 (2.1)
Ticlopidine	33 (1.1)*	19 (0.3)	3 (0)
Cilostazol	11 (0.4)*	71 (1.1)	115 (1.1)
Clopidogrel	5 (0.2)*	121 (1.8)	209 (2)
Others	–	14 (0.2)	175 (1.7)*
Dual therapy	–	5229 (78.9)	8104 (77.8)
ASA–TCL	1217 (40.9)	1022 (15.2)	151 (1.4)*
ASA–CLP	120 (4)	2608 (38.8)	5129 (49.2)*
ASA–CSZ	590 (19.8)	1354 (20.1)	1456 (14)*
CSZ–CLP	10 (0.3)	472 (7)	1326 (12.7)*
Others	–	281 (4.2)*	42 (0.4)
Triple or more	–	567 (8.4)	1231 (11.8)*
None	–	27 (0.4)	78 (0.7)*
Unknown	–	178 (2.6)	282 (2.7)
Post-procedural anticoagulant therapy			
Yes	–	4051 (60.2)*	5592 (53.7)
Heparin	1125 (37.8)	1468 (21.8)	1097 (10.5)*
Argatroban	1086 (36.5)	2570 (38.2)	4169 (40)*
Others	97 (3.3)	466 (7)	833 (8)
None	–	2399 (35.7)	4345 (41.7)*

*Indicates significant difference compared with others. ASA: aspirin, CSZ: cilostazol, PTA: percutaneous transluminal angioplasty, TCL: ticlopidine.

Changes in periprocedural antithrombotic therapy paradigms between JR-NET 1, 2, and 3

On analyzing all the cases that met the inclusion criteria, including aneurysms (ruptured/unruptured), PTA, and stenting, post-procedural anticoagulant therapy was less utilized in JR-NET 3 than in JR-NET 2 (53.9% vs. 60.6%, $P < 0.001$, Fig. 1A). Among the anticoagulants, heparin therapy remarkably decreased (12.7% vs. 23.4%, $P < 0.001$), argatroban therapy was same, and ozagrel therapy increased (7.5% vs. 5.8%, $P < 0.05$, Fig. 1B) in JR-NET 3.

Pre-procedural antiplatelet therapy became more frequent and more aggressive with each generation (Fig. 2A). The frequency of aggressive therapy (dual, and triple or more therapy) was 65.2% in JR-NET 3, which was significantly higher than in JR-NET 1

and 2 (41.5%, 61.2%, respectively, $P < 0.001$). The data of post-procedural antiplatelet therapy showed a significantly higher percentage in JR-NET 3 than in JR-NET 2 (66.6% vs. 56.6%, $P < 0.001$).

The rates of perioperative complications were compared between JR-NET 2 and 3 (Fig. 3). Ischemic complications (2.0% vs. 5.8%, $P < 0.001$) had significantly increased, whereas hemorrhagic complications had significantly decreased (5.3% vs. 2.1%, $P < 0.001$) in JR-NET 3. The rate of groin-site complications (0.7% vs. 1.0%, $P = 0.380$) and severe adverse events (2.0% vs. 2.1%, $P = 0.718$) showed no significant differences between both the groups. On the whole, the incidence of all perioperative complications were not significantly different between JR-NET 2 and 3 (10.3% vs. 10.9%, $P = 0.551$).
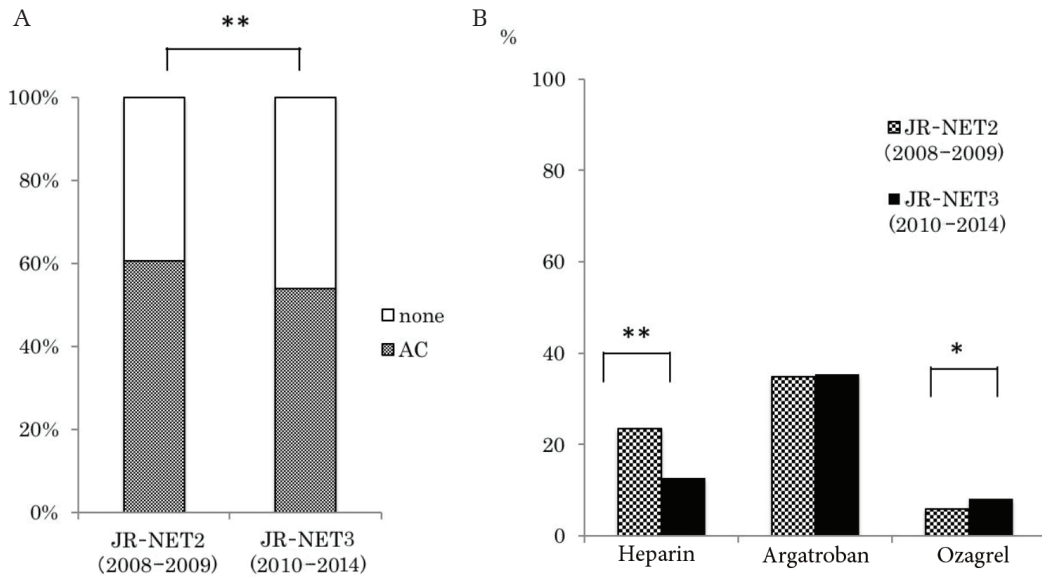
Fig. 1 Changes in post-procedural anti-coagulant therapy paradigms between JR-NET 2 and 3. (A) The proportion of patients who received post-procedural anticoagulants therapy. (B) The proportion of each anticoagulant used for the patients. AC: anti-coagulants, JR-NET: Japanese Registry of Neuroendovascular Therapy. *$P < 0.05$, **$P < 0.01$.
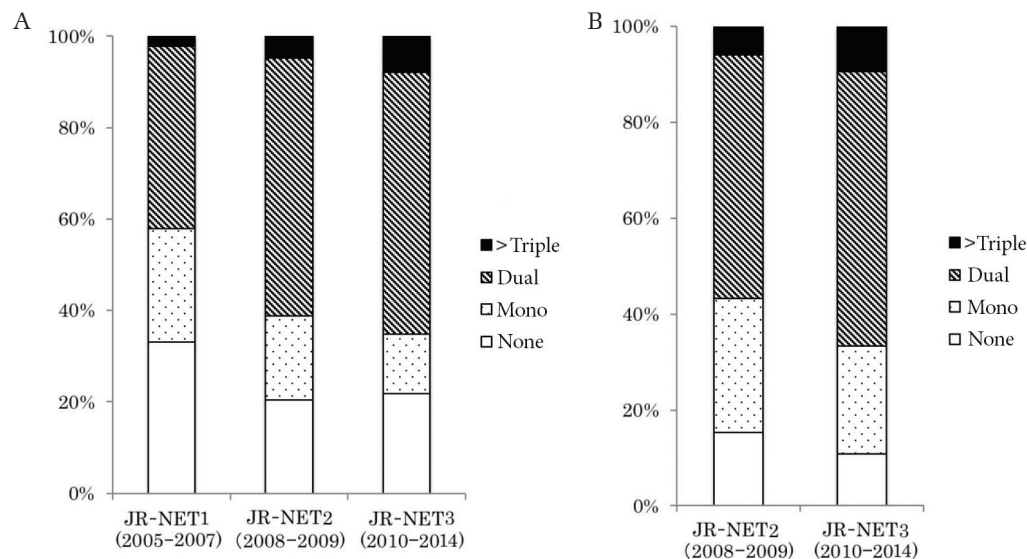
Fig. 2 Change in pre- and post-procedural antiplatelet therapy paradigms between JR-NET 1, 2, and 3. (A) The proportion of patients who received pre-procedural antiplatelet therapy. (B) The proportion of patients who received post-procedural antiplatelet therapy. JR-NET: Japanese Registry of Neuroendovascular Therapy.
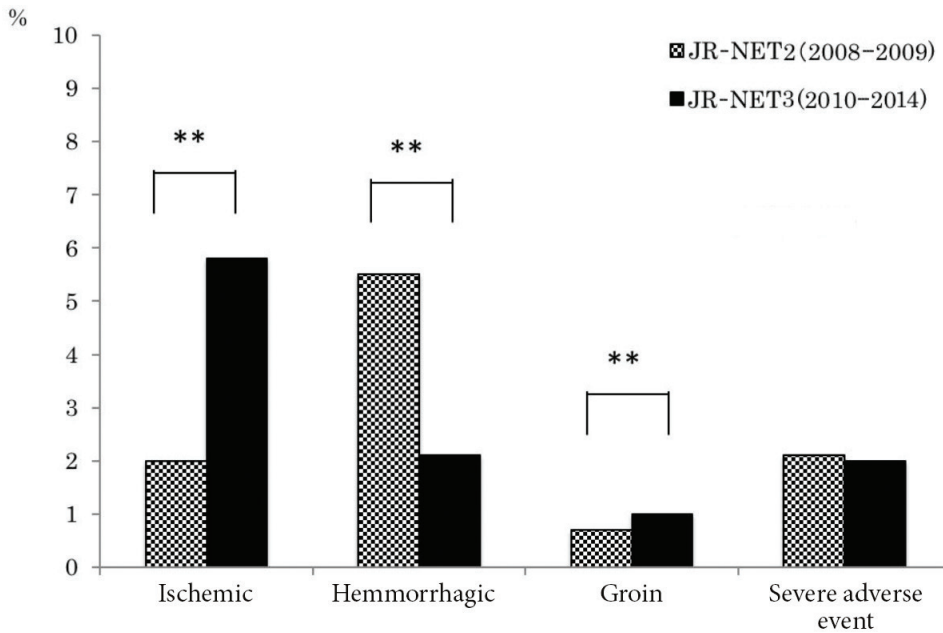
Fig. 3 Changes seen in the periprocedural complications in endovascular therapy to usually perform antithrombotic therapy between JR-NET 2 and 3. JR-NET: Japanese Registry of Neuroendovascular Therapy. **P <0.01.

Discussion

Thromboembolic events are the most common adverse events in neuroendovascular therapy. To reduce the number of thromboembolic events, antithrombotic therapy has been prescribed for neuroendovascular therapy. After Yamada et al.[4] reported that pre-procedural antiplatelet therapy reduced thromboembolic complications of aneurysm coiling, pre-procedural antiplatelet monotherapy was the commonly used regimen for unruptured aneurysm coiling. Afterward, several new devices such as intracranial stents, vascular remodeling devices for aneurysm coiling, and more recently, flow diverters, which have a higher metallic surface area and higher risk of in-stent thrombus formation, have been introduced. Currently, neuroendovascular therapy for aneurysms have changed to higher thromboembolic risk treatment; hence, periprocedural antithrombotic therapy has become more intensive to prevent the risk. In this study, the most common periprocedural antiplatelet regimen for unruptured aneurysms had changed from aspirin monotherapy to aspirin-clopidogrel dual therapy which is usually periprocedural antiplatelet regimen for stent-assisted coil embolization or flow diverter treatment.

These novel techniques and devices made wide-necked large aneurysms treatable, and extended the treatment indications to include more difficult and complicated aneurysms. In this study, we found that perioperative antithrombotic therapy was more focused on antiplatelet therapy than anticoagulant therapy. Antiplatelet therapy is more frequently

used with a greater number of multiple agents; however, periprocedural ischemic complications was significantly higher in JR-NET 3 than in JR-NET 1 and 2. These results might be attributed to the expanded treatment indications due to the development and approval of new devices or procedures. In Japan, carotid artery stents have been approved in 2007, that is a border of JR-NET 1 and 2. Before the approval, carotid artery stenting had been only indicated for the limited, small number of patients under off-label use. However, after the approval, the number of cases has been increasing year-by-year. Although the number of the procedures of carotid artery stenting in JR-NET 2 (after approval generation) had increased 2.5 times as high as JR-NET 1 (before approval generation), the rate of procedure-related complication and morbidity was slightly higher in JR-NET 2 than JR-NET 1.[5] The same phenomenon might be observed in aneurysm treatment, because vascular remodeling devices for cerebral aneurysm that have a potential risk of in-stent thrombosis or procedure-related thrombo-embolic complication[6] have been approved in 2010, that is a border of JR-NET 2 and 3. In JR-NET 3, about 20% cases of unruptured aneurysm were treated by stent-assisted coil embolization.

As another expected reason for the increasing of ischemic complication despite of aggressive antiplatelet therapy, the increase in the number of neuro-interventionalists might be considered. The number of board-certificated surgeons of Japanese Society of Neuroendovascular Therapy is increasing year-by-year, now over 1300 surgeons. As surgeons increase, the technical level might tend to decrease.

With respect to PTA or stenting, after the 2007-consensus document for carotid artery stenting that recommended periprocedural dual antiplatelet therapy,[7] aspirin-clopidogrel dual therapy became the common regimen. Dual therapy combinations with clopidogrel, a second generation thienopyridine with P2Y12-receptor inhibitor, were widely used for coronary interventions due to its efficacy for preventing in-stent thrombosis.[8] However, it has a problem of its variability in pharmacological, genetic or clinical. Clopidogrel is a prodrug that requires metabolism for conversion to its active metabolite that depends on hepatic cytochrome p-450 (CYP) 2C19. Japanese have a higher frequency of poor metabolizer CYP2C19 genotype polymorphism than other races[9]; this would mean that Japanese individuals must take note of hypo-responders of clopidogrel and consequent risk of ischemic events.[10,11] Several adjunctive treatments were proposed for the hypo-responder; triple therapy combination with cilostazol demonstrated efficacy in reducing the rate of high-on treatment platelet reactivity and periprocedural events.[12] This situation might influence the increasing ratio of triple therapy in this study. Subsequently, these clinical implications led to the development of more effective P2Y12 inhibitors, prasugrel (third-generation thienopyridine) and ticagrelor (cyclopentyl-triazolo-pyrimidine); these drugs provide more consistent, rapid, and potent platelet inhibition than clopidogrel,[13–15] based on the concept that "stronger is better". Nevertheless, stronger efficacy increases the risk of hemorrhagic complications. In addition, a meta-analysis of antiplatelet therapy in acute ischemic stroke revealed that long-term dual therapy does not reduce the risk of stroke recurrence and is associated with an increased risk of major bleeding events.[16] In our previous study,[3] intensive periprocedural antithrombotic therapy reduced the ischemic complications but increased hemorrhagic complications, especially with the use of triple or more therapy.

Therefore, a new challenge is to individualize optimal antithrombotic therapy to decrease thrombotic events without increasing bleeding. In the field of coronary intervention, several detailed guidelines for periprocedural antithrombotic management have been already published.[17,18] Although the optimal antithrombotic therapy for neuroendovascular treatment is still unclear, platelet function monitoring to evaluate individual response to antiplatelet agents is effective to prevent thromboembolic and hemorrhagic complications.[19] Tailor-made antiplatelet therapy based on platelet function monitoring may become one of the solutions for optimal antithrombotic therapy in neuroendovascular treatment. As if to reflect this

situation, hemorrhagic complication was less in JR-NET 3 in spite of aggressive antiplatelet therapy.

Regarding post-procedural anticoagulation therapy for neuroendovascular treatment, there is no evidence of its effectiveness in preventing periprocedural events by themselves. In the 1990s, standard periprocedural antithrombotic therapy comprised anticoagulant therapy with heparin or warfarin and aspirin monotherapy in coronary intervention; however, subacute stent thrombosis frequently occurred and was considered a serious problem. A randomized trial that compared dual antiplatelet therapy versus aspirin plus anticoagulant therapy showed that dual antiplatelet therapy significantly reduced subacute stent thrombosis.[20] As a result, the superiority of antiplatelet therapy became common knowledge. In this study, the ratio of post-procedural anticoagulant therapy had reduced with each generation.

This study has several limitations. We retrospectively analyzed different endovascular procedures collectively, but the ratio of each different procedures is different in each generation. And this study lacked the data of the duration of antithrombotic therapy and the details of procedures. Moreover, the decision to initiate neuroendovascular treatment or periprocedural antithrombotic therapy was decided independently at each facility. These factors might affect the periprocedural complications and the indications for post-procedural antithrombotic therapy.

Conclusion

In this study, we found that periprocedural antiplatelet therapy was more frequently used with a large number of multiple agents, and periprocedural anticoagulant therapy was less frequently used in neuroendovascular therapy in Japan compared with previous generations. Despite a strong antiplatelet regimen, Ischemic complications increased and hemorrhagic complications decreased. Future prospective studies are warranted to identify the actual effects of periprocedural antithrombotic therapy on periprocedural complications.

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Conflicts of Interest Disclosure

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