Original Article doi: 10.2176/nmc.oa.2018-0325

Neurol Med Chir (Tokyo) 59, 305–312, 2019 Online May 25, 2019

Safety and Feasibility of Neuroendovascular Therapy for Elderly Patients: Analysis of Japanese Registry of Neuroendovascular Therapy 3

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Abstract

Japan has a rapidly aging population and the application of neuroendovascular therapy (NET) for cerebrovascular diseases among elderly patients has increased, but feasibility and safety of NET for elderly patients are still debated. Therefore, this study aimed to elucidate feasibility and safety of NET by analyzing the Japanese nationwide database, the Japanese Registry of Neuroendovascular Therapy 3 (JR-NET 3). In total, 35,972 patients in the JR-NET 3 were analyzed retrospectively. "Elderly patients" were defined as those aged ≥75 years. Approximately one-quarter of patients who received NET were elderly patients. The proportion of patients with modified Rankin Scale (mRS) 0–2 before treatment and 30 days after NET was significantly low across all diseases in the elderly patients. Technical success rates were generally high across all procedures, but complication rate was significantly higher among elderly patients; ischemic complications were significantly higher with NET for unruptured aneurysms (UA) and carotid artery stenosis (CAS). Multivariate analysis revealed that mRS 0–2 before treatment [odds ratio (OR): 0.56, 95% confidence interval (CI): 0.34–0.94, *P* = 0.03], middle cerebral artery aneurysm (OR: 0.33, 95% CI: 0.12–0.92, *P* = 0.04), and complete obliteration (OR: 0.66, 95% CI: 0.44–0.97, *P* = 0.03) were associated with ischemic complications with NET for UA. Moreover, mRS 0–2 before treatment (OR: 0.55, 95% CI: 0.36–0.86, *P* < 0.01), high intensity with time-of-flight magnetic resonance angiography (OR: 1.55, 95% CI: 1.03–2.32, *P* = 0.04), open-cell stent (OR: 2.20, 95% CI: 1.50–3.22, *P* <0.01) were associated with ischemic complications with NET for CAS. Taken together, our findings indicate that cautious and precise selection of patients suitable for NET is necessary.

Key words: neuroendovascular therapy, JR-NET 3, elderly

Introduction

As Japan has a rapidly aging population, the prevalence of cerebrovascular disease in elderly patients, and consequently, the use of neuroendovascular therapy (NET) for its treatment has increased. Although the application of NET is reportedly feasible and safe for elderly patients,[1–5] a precise indication of the procedure is required on account of the many risk factors involved. The Japanese Registry of Neuroendovascular Therapy 3 (JR-NET 3), a Japanese nationwide database was created as a sequel to the JR-NET 1 and 2.[6–21] To better elucidate the safety and efficacy profiles associated with NET for elderly patients, we conducted a detailed analysis of JR-NET 3.

Materials and Methods

A total of 40,177 patients who underwent NET in Japan were enrolled in the JR-NET 3 from January 2010 to December 2014. Of the 36,708 patients with information of periprocedural status and treatment available, 736 patients without age description were

Received December 28, 2018; Accepted April 1, 2019

excluded; this analysis thus included 35,972 patients. The data were collected from the certificated board members of Japanese Society for Neuroendovascular Therapy. The Institutional Review Board at each center approved the use of retrospective data from the patients.

We defined "elderly patients" as those aged ≥75 years. We collected the following patient information: baseline characteristics [age, sex, diagnosis, and modified Rankin Scale (mRS) before treatment, characteristics of the aneurysm, site of the aneurysm, plaque characteristics], procedures (kind of procedure, anesthesia, technical success, doctor responsible for treatment, embolization-assisted devices, protection devices, types of the stents, preoperative antiplatelet agent, procedural complications); and outcome (mRS at 30 days after treatment). Technical success rate was defined as the rate at which treatment purpose was achieved completely or partially. We also analyzed the aforementioned data in relation to the diseases the patients had. Diseases considered included unruptured aneurysms (UA), ruptured aneurysms (RA), acute ischemic stroke (AIS), carotid artery stenosis (CAS), and intracranial artery stenosis (ICAS). For patients with UA or RA, only intrasaccular embolization was analyzed.

Additionally, we investigated types of complications concomitant with each disease, such as hemorrhagic and ischemic complications, puncture site complications, cholesterol embolisms, and other systemic complications. We performed univariate and multivariate analyses to investigate the risk factors for each complication.

Statistical analyses

All analyses were performed with JMP Statistical Software, version 13 (SAS Institute Inc., Cary, NC, USA). For the univariate analysis, nominal and continuous variables were examined using the chi-square test and the unpaired *t*-test. For the multivariate analysis, multiple logistic regression analysis was adopted. A *P*-value of <0.05 was considered statistically significant for each test.

Results

The mean and median ages of the enrolled patients were 65.1 and 68 years, respectively. Characteristics of patients and treatments, and results of the procedure were shown in Table 1. The proportion of the elderly patients was 27.7%, and was higher in patients treated by NET for AIS and CAS than ruptured RA and UA. To elucidate the feasibility of NET for the elderly patients, we further investigated the technical success rate of the procedures. Technical success rates were generally high for all procedures including those in the elderly patients; however, there was a significant difference for all patients, particularly in AIS.

We also analyzed the mRS to investigate the pre and postoperative status of the patients before treatment and 30 days after the treatment. Across all types of diseases, the proportions of patients with mRS scores of 0–2 in the elderly patients were significantly lower than those of their counterparts at both time points.

We further examined the perioperative complications of NET (Table 2). It was revealed that the rates of hemorrhagic, ischemic, and other systemic complications were significantly higher in NET for the elderly patients. On the other hand, the complication rates among the elderly patients did not increase in cases of RA, AIS, and ICAS. In particular, we found that ischemic complication rates in the elderly patients increased significantly among cases of UA and CAS, but decreased among cases of AIS.

Finally, we investigated the risk factors for ischemic complications with NET for UA and CAS in the elderly patients (Tables 3 and 4). Multivariate analysis revealed that patients with mRS 0–2 before treatment [odds ratio (OR): 0.56, 95% confidence interval (CI): 0.34–0.94, $P = 0.03$], middle cerebral artery (MCA) aneurysm (OR: 0.33, 95% CI: 0.12–0.92, $P = 0.04$), and complete obliteration (OR: 0.66, 95% CI: 0.44–0.97, $P = 0.03$) were significantly associated with ischemic complications with NET for UA. On the other hand, patients with mRS 0–2 before treatment (OR: 0.55, 95% CI: 0.36–0.86, $P < 0.01$), high intensity of the plaque with time-of-flight magnetic resonance angiography (OR: 1.55, 95% CI: 1.03–2.32, $P = 0.04$), and open-cell stent (OR: 2.20, 95% CI: 1.50–3.22, $P < 0.01$) were significantly associated with ischemic complications with NET for CAS.

Discussion

Concomitant with the aging of the Japanese population, NET is being increasingly performed on the elderly patients in Japan. However, as elderly people are subject to various risk factors, the indications of NET needs to be carefully considered. The present study, however, demonstrated the feasibility and safety of NET for elderly patients by analyzing data from the JR-NET 3.

We found that approximately one-quarter of patients who received NET were aged 75 years or older (Table 1); the proportion of the elderly patients with UA was low, whereas over 40% of

Table 1 Characteristics of patients, treatments, and results of the procedure

	<75 y (*n* = 26,025)	≥75 y (*n* = 9947)	*P*-value
Age, mean ± SD	59.5 ± 12.5	80.2 ± 4.3	
Sex: Female, *n* (%)	12,689 (48.8)	4671 (47.0)	
Types of procedure, *n* (%)			
All procedure (*n* = 35,972)	26,025 (72.3)	9947 (27.7)	
Ruptured AN (*n* = 5866)	4158 (70.9)	1708 (29.1)	
Unruptured AN (*n* = 10,070)	8788 (87.3)	1282 (12.7)	
Acute ischemic stroke (*n* = 3897)	2085 (53.5)	1812 (46.5)	
Carotid artery stenosis (*n* = 8388)	4682 (55.8)	3706 (44.2)	
Intracranial artery stenosis (*n* = 975)	666 (68.3)	309 (31.7)	
Technical success rate, %			
All procedures	97.6	96.1	<0.01*
Ruptured AN	98.4	97.8	0.19
Unruptured AN	97.9	97.2	0.13
Acute ischemic stroke	89.1	86.1	<0.01*
Carotid artery stenosis	99.1	98.9	0.58
Intracranial artery stenosis	98.2	96.1	0.07
Proportion of mRS 0–2 before and after treatment, %			
All procedures			
Before treatment	88.7	79.0	<0.01*
30 days after treatment	72.8	54.0	<0.01*
Ruptured AN			
Before treatment	90.8	75.5	<0.01*
30 days after treatment	57.1	22.4	<0.01*
Unruptured AN			
Before treatment	96.2	89.3	<0.01*
30 days after treatment	93.3	80.0	<0.01*
Acute ischemic stroke			
Before treatment	88.2	74.4	<0.01*
30 days after treatment	23.2	12.8	<0.01*
Carotid artery stenosis			
Before treatment	87.9	84.1	<0.01*
30 days after treatment	82.1	76.0	<0.01*
Intracranial artery stenosis			
Before treatment	85.3	70.0	<0.01*
30 days after treatment	79.0	56.6	<0.01*

*Statistically significant. AN: aneurysm, mRS: modified Rankin Scale, y: years.

the procedures could be accounted for by AIS and CAS. Although the elderly patients are more prone to these diseases, it is necessary to only select patients who can safely receive NET. Additionally, this study demonstrated that both pre and postoperative condition of the elderly patients were significantly worse across all types of diseases (Table 1). It is considered that elderly patients tended to deteriorate due to problems such as general conditions; however, there is a possibility that the proportion of NET was increased in the elderly, which might affect the difference in postoperative condition. Taken together, indications of NET for the elderly patients should be considered carefully.

Table 2 Periprocedural complications

	Age		*P*-value
	<75 y	≥75 y	
All patients, *n* (%)	*n* = 26,025	*n* = 9947	
All complications	2475 (9.5)	1097 (11.0)	<0.01*
Hemorrhagic	693 (2.7)	322 (3.2)	<0.01*
Ischemic	1277 (4.9)	547 (5.5)	0.02
Puncture site	211 (0.8)	84 (0.8)	0.74
Cholesterol embolism	9 (0.03)	2 (0.02)	0.74
Other systemic	49 (0.19)	34 (0.34)	<0.01*
Ruptured AN, *n* (%)	*n* = 4158	*n* = 1708	
All complications	543 (13.1)	218 (12.8)	0.80
Hemorrhagic	181 (4.4)	73 (4.3)	0.94
Ischemic	341 (8.2)	130 (7.6)	0.14
Puncture site	11 (0.3)	2 (0.1)	0.37
Cholesterol embolism	0	0	–
Other systemic	2 (0.05)	2 (0.12)	0.59
Unruptured AN, *n* (%)	*n* = 8788	*n* = 1282	
All complications	840 (9.6)	190 (14.8)	<0.01*
Hemorrhagic	176 (2.0)	20 (1.6)	0.33
Ischemic	470 (5.3)	140 (10.9)	<0.01*
Puncture site	117 (1.3)	15 (1.2)	0.79
Cholesterol embolism	0	0	–
Other systemic	6 (0.07)	3 (0.23)	0.10
Acute ischemic stroke, *n* (%)	*n* = 2085	*n* = 1812	
All complications	281 (13.5)	231 (12.7)	0.51
Hemorrhagic	186 (8.9)	169 (9.3)	0.70
Ischemic	64 (3.1)	30 (1.7)	<0.01*
Puncture site	9 (0.4)	13 (0.7)	0.29
Cholesterol embolism	1 (0.05)	0 (0)	1
Other systemic	5 (0.24)	10 (0.55)	0.13
Carotid artery stenosis, *n* (%)	*n* = 4682	*n* = 3706	
All complications	338 (7.2)	333 (9.0)	<0.01*
Hemorrhagic	40 (0.9)	25 (0.7)	0.38
Ischemic	178 (3.8)	195 (5.3)	<0.01*
Puncture site	52 (1.1)	43 (1.2)	0.84
Cholesterol embolism	7 (0.15)	3 (0.08)	0.53
Other systemic	24 (0.51)	21 (0.57)	0.76
Intracranial artery stenosis, *n* (%)	*n* = 666	*n* = 309	
All complications	76 (11.4)	33 (10.7)	0.83
Hemorrhagic	20 (3.0)	9 (2.9)	1
Ischemic	37 (5.6)	13 (4.2)	0.44
Puncture site	5 (0.8)	1 (0.3)	0.67
Cholesterol embolism	0	0	–
Other systemic	1 (0.15)	3 (0.97)	0.10

*Statistically significant. AN: aneurysm, y: years.

Table 3 Risk factors for ischemic complications with NET for UA in elderly patients

	Univariate analysis	Multivariate analysis	
	P-value	Odds ratio (95% CI)	*P*-value
Patient characteristics			
Age ≥80	0.62		
Sex: Female	0.38		
mRS 0–2 before treatment	0.01	0.56 (0.34–0.94)	0.03*
Characteristics of AN			
Symptomatic	0.04	1.34 (0.87–2.05)	0.18
≥10 mm	0.33		
Site of AN			
ICA	1		
ACA	0.57		
MCA	0.06	0.33 (0.12–0.92)	0.04*
Posterior circulation	0.03	1.23 (0.80–1.90)	0.34
Procedure			
General anesthesia	0.43		
Balloon-assisted	<0.01	0.65 (0.41–1.04)	0.07
Stent-assisted	<0.01	1.43 (0.93–2.20)	0.11
Proximal balloon protection	0.52		
Complete obliteration	0.03	0.66 (0.44–0.97)	0.03*
Preoperative antiplatelet therapy			
DAPT	0.39		
Aspirin	0.80		
Clopidogrel	0.64		
Cilostazol	0.62		

*Statistically significant. ACA: anterior cerebral artery, AN: aneurysm, DAPT: dual antiplatelet therapy, ICA: internal carotid artery, MCA: middle cerebral artery, mRS: modified Rankin Scale, NET: neuroendovascular therapy, UA: unruptured aneurysm.

Table 4 Risk factors for ischemic complications with CAS in elderly patients

	Univariate analysis	Multivariate analysis	
	P-value	Odds ratio (95% CI)	*P*-value
Patient characteristics			
Age ≥80	0.16	1.18 (0.82–1.70)	0.37
Female	0.67		
mRS 0–2 before treatment	0.09	0.55 (0.36–0.86)	<0.01
Plaque characteristics			
Symptomatic lesion	0.33		
Echolucent	0.16	1.26 (0.83–1.90)	0.28
TOF high	0.15	1.55 (1.03–2.32)	0.04*
Procedure			
General anesthesia	0.41		
Filter protection	0.06	1.31 (0.91–1.89)	0.15

(*Continued*)

Table 4 (Continued)

	Univariate analysis	Multivariate analysis	
	P-value	Odds ratio (95% CI)	*P*-value
Distal balloon protection	0.30		
Proximal balloon protection	0.52		
Open-cell stent	<0.01	2.20 (1.50–3.22)	<0.01*
Residual stenosis ≥50%	0.03	1.45 (0.33–6.30)	0.62
Preoperative antiplatelet therapy			
DAPT	1		
Aspirin	0.34		
Clopidogrel	0.12	0.80 (0.53–1.22)	0.30
Cilostazol	0.50		

*Statistically significant. CAS: carotid artery stenting, DAPT: dual antiplatelet therapy, mRS: modified Rankin Scale, TOF: time-of-flight magnetic resonance angiography.

We investigated the feasibility of NET for the elderly patients by assessing the technical success rate of the procedures (Table 1). It was revealed that the technical success rates of procedures among the elderly patients exceeded 90% across almost all diseases; a significant difference was observed in the success rates of AIS treatment in the elderly and younger patients. Although the reason is unclear, several technical difficulties, such as anatomical challenges involving tortuosity and stenosis of the vessels, and restlessness during the procedure may have arisen, while NET was performed on the elderly patients with atherosclerotic disease. As we usually do not have adequate anatomical information before initiating treatment for AIS, the technical success rate of AIS treatment in elderly patients might be significantly lower than that in younger patients. Therefore, it may be necessary to take precautions specific to elderly patients when preparing the devices and drugs used when performing NET.

This study also found that the rate of complication was significantly higher than their younger counterparts among cases of UA and CAS in the elderly. However, this was not true for cases of RA, AIS, and ICAS in the elderly when compared with their younger counterparts (Table 2). Moreover, it is notable that ischemic complications were significantly higher among cases of UA and CAS but not among cases of AIS. Multiple reports on the risk of NET for elderly patients have suggested that the safety of NET for the elderly patients depends on the disease being treated. For example, age was found to be a more salient risk factor for carotid artery stenting than for carotid endarterectomy[5,21]; however, it has been shown that the benefits of performing mechanical thrombectomy using a stent retriever remain among patients >80 years of age.[1] From the analysis in this study, we concluded that special attention needed to be given to the ischemic complications when performing NET for UA and CAS in the elderly patients. On the other hand, NET for the elderly patients with RA, AIS, and ICAS might be acceptable.

Whether age is a predictor of poor outcome when NET is used to treat unruptured aneurysms is subject to debate. Oishi et al.[22] observed that poor outcome was not related to age and concluded that old age should not be a contraindication. Wiebers et al.[3] have reported that age was a strong predictor of surgical outcome but not of endovascular outcome. In contrast, Brinjikji et al.[23] found that increasing age was associated with a higher probability of combined neurological morbidity and mortality in aneurysm embolization with flow diverters. In this study, ischemic complications were increased significantly in the elderly patients than their younger counterparts with NET for UA. Since ischemic complication was decreased significantly in patients with mRS 0–2 before treatment, MCA aneurysm, and complete obliteration, on multivariate analysis, these factors should be considered when performing NET for UA in the elderly patients (Table 3). Furthermore, only 89.3% of the elderly patients with UA were in good preoperative condition with mRS 0–2, and the remaining patients with poor preoperative condition should not be treated. Taking into consideration that the rupture risk of unruptured aneurysm in the elderly patients is about 3.6%,[24] indication of NET for UA in the elderly patients should be decided strictly.

Prior research has already suggested that age is a strong predictor of poor outcome in cases of carotid artery stenting.[5,21] Our results were consistent with these reports: ischemic complications were

observed to be increased among elderly patients. In addition, poor preoperative condition with mRS > 2, vulnerable plaque with hyperintensity signal on time-of-flight magnetic resonance angiography, and usage of open-cell stent were the risk factors for ischemic complications of NET for CAS in the elderly patients. These factors should be considered to prevent ischemic complications in performing carotid artery stenting for them.

This study is subject to several limitations, among which are those inherent to the retrospective nature of the study. In addition, some age data were missing and our sample size was thus narrowed. Furthermore, complications and outcomes were evaluated by treatment physicians who were not blinded. Despite these limitations, this study determined the current status of NET in Japan and clarified the problems of NET for the elderly patients.

In summary, this study found that NET for the elderly patients is relatively feasible and safe, but ischemic complications were increased significantly among cases of UA and CAS. Our findings emphasize the need to prevent complications with NET for the elderly patients, by selecting patients suitable for the procedure with care and performing the procedure with caution, especially in the embolization of unruptured aneurysms and carotid artery stenting.

Acknowledgments

This study was supported in part by a Grant-in-Aid (Junkanki-Kaihatsu H24-4-3) from the National Cerebral and Cardiovascular Center, Japan and by Hatazaki Foundation, Kobe, Japan.

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Conflicts of Interest Disclosure

N. Sakai received Speakers' Bureau/Honoraria from Otsuka Pharmaceutical Co., Stryker Co., Medtronic Co., Medico's Hirata Co., and Biomedical Solutions Co., and research funding from Otsuka Pharmaceutical Co., Terumo Co., and Daiichi Sankyo Co. K. Iihara received Speakers' Bureau/Honoraria from Otsuka Pharmaceutical Co., and research funding from Otsuka Pharmaceutical Co., Mitsubishi Tanabe Pharma Co., Kaneka Medix Co., Chugai Pharmaceutical Co., and Eizai Co. K. Arimura, T. Sato, A. Nishimura, and S. Tokunaga had no conflicts of interest to declare. All authors who are members of the Japan Neurosurgical Society (JNS) have registered online Self-reported COI Disclosure Statement Forms through the website for JNS members.

References

1) Goyal M, Menon BK, van Zwam WH, et al.: Endovascular thrombectomy after large-vessel ischaemic stroke: a meta-analysis of individual patient data from five randomised trials. *Lancet* 387: 1723–1731, 2016
2) Sturiale CL, Brinjikji W, Murad MH, Lanzino G: Endovascular treatment of intracranial aneurysms in elderly patients: a systematic review and meta-analysis. Stroke 44: 1897–1902, 2013
3) Wiebers DO, Whisnant JP, Huston J, et al.: Unruptured intracranial aneurysms: natural history, clinical outcome, and risks of surgical and endovascular treatment. *Lancet* 362: 103–110, 2003
4) Ryttlefors M, Enblad P, Kerr RS, Molyneux AJ: International subarachnoid aneurysm trial of neurosurgical clipping versus endovascular coiling: subgroup analysis of 278 elderly patients. *Stroke* 39: 2720–2726, 2008
5) Howard G, Roubin GS, Jansen O, et al.: Association between age and risk of stroke or death from carotid endarterectomy and carotid stenting: a meta-analysis of pooled patient data from four randomised trials. *Lancet* 387: 1305–1311, 2016

6) Hiramatsu M, Sugiu K, Hishikawa T, et al.: Epidemiology of dural arteriovenous fistula in Japan: analysis of Japanese Registry of Neuroendovascular Therapy (JR-NET2). *Neurol Med Chir* (*Tokyo*) 54: 63–71, 2014
7) Shigematsu T, Fujinaka T, Yoshimine T, et al.: Endovascular therapy for asymptomatic unruptured intracranial aneurysms: JR-NET and JR-NET2 findings. *Stroke* 44: 2735–2742, 2013
8) Sakai N, Yoshimura S, Taki W, et al.: Recent trends in neuroendovascular therapy in Japan: analysis of a nationwide survey—Japanese Registry of Neuroendovascular Therapy (JR-NET) 1 and 2. *Neurol Med Chir* (*Tokyo*) 54: 1–8, 2014
9) Hishikawa T, Sugiu K, Hiramatsu M, et al.: Nationwide survey of the nature and risk factors of complications in embolization of meningiomas and other intracranial tumors: Japanese Registry of NeuroEndovascular Therapy 2 (JR-NET2). *Neuroradiology* 56: 139–144, 2014
10) Ishii A, Miyamoto S, Ito Y, Fujinaka T, Sakai C, Sakai N: Parent artery occlusion for unruptured cerebral aneurysms: The Japanese Registry of Neuroendovascular Therapy (JR-NET) 1 and 2. *Neurol Med Chir* (*Tokyo*) 54: 91–97, 2014
11) Enomoto Y, Yoshimura S, Sakai N, Egashira Y; Japanese Registry of Neuroendovascular Therapy (JR-NET) investigators: Current perioperative management of anticoagulant and antiplatelet use in neuroendovascular therapy: analysis of JR-NET1 and 2. *Neurol Med Chir* (*Tokyo*) 54: 9–16, 2014
12) Satow T, Ishii D, Iihara K, Sakai N; JR-NET Study Group: Endovascular treatment for ruptured vertebral artery dissecting aneurysms: results from Japanese Registry of Neuroendovascular Therapy (JR-NET) 1 and 2. *Neurol Med Chir* (*Tokyo*) 54: 98–106, 2014
13) Kikuchi T, Ishii A, Nakahara I, Miyamoto S, Sakai N: Japanese Registry of Neuroendovascular Therapy: extracranial steno-occlusive diseases except for internal carotid artery stenosis. *Neurol Med Chir* (*Tokyo*) 54: 40–45, 2014
14) Tsuruta W, Matsumaru Y, Miyachi S, Sakai N: Endovascular treatment of spinal vascular lesion in Japan: Japanese Registry of Neuroendovascular Therapy (JR-NET) and JR-NET2. *Neurol Med Chir* (*Tokyo*) 54: 72–78, 2014
15) Kondo R, Matsumoto Y, Endo H, Miyachi S, Ezura M, Sakai N: Endovascular embolization of cerebral arteriovenous malformations: results of the Japanese Registry of Neuroendovascular Therapy (JR-NET) 1 and 2. *Neurol Med Chir* (*Tokyo*) 54: 54–62, 2014
16) Hayakawa M, Yamagami H, Sakai N, Matsumaru Y, Yoshimura S, Toyoda K: Endovascular treatment of acute stroke with major vessel occlusion before approval of mechanical thrombectomy devices in Japan: Japanese Registry of Neuroendovascular Therapy (JR-NET) and JR-NET 2. *Neurol Med Chir* (*Tokyo*) 54: 23–31, 2014
17) Sato M, Matsumaru Y, Sakai N, Yoshimura S; JR-NET Study Group Affiliations: Detailed analysis of puncture site vascular complications in Japanese Registry of Neuroendovascular Therapy (JR-NET) and JR-NET2. *Neurol Med Chir* (*Tokyo*) 54: 17–22, 2014
18) Izumi T, Imamura H, Sakai N, Miyachi S: Angioplasty and stenting for intracranial stenosis. *Neurol Med Chir* (*Tokyo*) 54: 46–53, 2014
19) Hayashi K, Hirao T, Sakai N, Nagata I: Current status of endovascular treatment for vasospasm following subarachnoid hemorrhage: analysis of JR-NET2. *Neurol Med Chir* (*Tokyo*) 54: 107–112, 2014
20) Imamura H, Sakai N, Sakai C, Fujinaka T, Ishii A; JR-NET Investigators: Endovascular treatment of aneurysmal subarachnoid hemorrhage in Japanese Registry of Neuroendovascular Therapy (JR-NET) 1 and 2. *Neurol Med Chir* (*Tokyo*) 54: 81–90, 2014
21) Egashira Y, Yoshimura S, Sakai N, Enomoto Y; Japanese Registry of Neuroendovascular Therapy Investigators: Real-world experience of carotid artery stenting in Japan: analysis of 7,134 cases from JR-NET1 and 2 nationwide retrospective multi-center registries. *Neurol Med Chir* (*Tokyo*) 54: 32–39, 2014
22) Oishi H, Yamamoto M, Nonaka S, et al.: Treatment results of endosaccular coil embolization of asymptomatic unruptured intracranial aneurysms in elderly patients. *J Neurointerv Surg* 7: 660–665, 2015
23) Brinjikji W, Rabinstein AA, Lanzino G, Kallmes DF, Cloft HJ: Effect of age on outcomes of treatment of unruptured cerebral aneurysms: a study of the National Inpatient Sample 2001–2008. *Stroke* 42: 1320–1324, 2011
24) Hishikawa T, Date I, Tokunaga K, et al.: Risk of rupture of unruptured cerebral aneurysms in elderly patients. *Neurology* 85: 1879–1885, 2015

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