Can Periprocedural Hypotension in Carotid Artery Stenting Be Predicted?

A Carotid Morphologic Autonomic Pathologic Scoring Model Using Virtual Histology to Anticipate Hypotension

A. TSURUMI, S. MIYACHI, O. HOSOSHIMA, T. IZUMI, T. OHSHIMA, N. MATSUBARA, T. KINKORI, T. NAITO, T. WAKABAYASHI

Department of Neurosurgery, Nagoya University Graduate School of Medicine; Nagoya, Japan

Key words: carotid stenosis, stenting, carotid ultrasound, interventional neuroradiology, pathology, Virtual Histology

Summary

Periprocedural hypotension, which frequently occurs during carotid artery stenting (CAS), is an important risk factor for complications such as stroke or death after CAS.

To determine if a scoring model can be established to predict periprocedural hypotension (systolic blood pressure < or = 90 mm Hg) and prolonged periprocedural hypotension (requiring vasopressor for > 3 hours) in CAS, we conducted a prospective cohort study of patients undergoing interventional treatment of cervical carotid artery stenosis in an urban tertiary referral hospital from April 2006 to April 2007.

Forty-eight stenotic lesions in 45 consecutive patients treated with CAS were included in the study. Multivariate analysis showed three independent risk factors of periprocedural hypotension; "fibrous plaque on Virtual Histology" (P = 0.029), "stenotic lesion involving both the common carotid artery and internal carotid artery on angiogram" (P = 0.004), and "patients without history of diabetes mellitus" (P = 0.020). Further, "distance between carotid bifurcation and point of minimum lumen size < or = 10 mm on angiogram" (P = 0.003) was an independent risk factor of prolonged periprocedural hypotension. Carotid morphologic autonomic pathologic score (carotid MAPS), determined by adding one point for each of those risk factors (total 0 to 4), had good discrimination for both periprocedural hypotension (area under receiver operating characteristic curve: ROC AUC = 0.876; SE 0.053) and prolonged periprocedural hypotension (ROC AUC = 0.811; SE 0.066).

Carotid MAPS is useful for predicting periprocedural hypotension and prolonged periprocedural hypotension during CAS.

Introduction

Carotid artery stenting (CAS) of cervical carotid artery stenosis has been increasingly used as an alternative to carotid endarterectomy (CEA) [1]. Several studies [2-11] have shown that periprocedural hypotension is more frequent in CAS because CAS involves manipulation in the vicinity of both the adventitial baroreceptors and the carotid sinus. Periprocedural hypotension increases in-hospital complications and long-term risk of death after CAS [3,4]. Therefore, predictive factors for hypotension have been evaluated in many studies [3-10]. Predicting which patients are at high-risk for periprocedural hypotension will enable us to pre-treat them aggressively. This may, as a result, improve their prognoses.

Several studies of coronary [12-14] and carotid [15] artery plaque imaging have demonstrated that virtual histology (VH; Volcano Corporation, Rancho Cordova, CA), which is based on spectral and amplitude analyses of the intravascular ultrasound (IVUS) radiofrequency (RF) bac-

kscatter signals, allows reliable identification of four atherosclerotic plaque types: fibrous, fibrofatty, dense calcium, and necrotic core. In addition, the geometric and compositional output of VH IVUS has been reported to be reproducible [16]. Therefore, VH IVUS has been applied to the evaluation of plaque characteristics in both coronary interventions [17,18] and neurointerventions [19-21]. Periprocedural hypotension in CAS may be predicted by analyzing the plaque composition derived from VH IVUS.

The present study had three main aims, first it sought to determine the risk factors for periprocedural hypotension based on VH IVUS, second the study aimed to develop an accurate and simple scoring model. The third aim was to evaluate the effectiveness of the scoring model for the prediction of periprocedural hypotension in CAS.

Methods

Study Design

We conducted a prospective cohort study of the patients who underwent interventional therapy for cervical carotid artery stenosis in Nagoya University Hospital from April 1, 2006 to April 30, 2007. This hospital is a tertiary referral center of Nagoya, a city of 2.2 million people in central Japan. This neurosurgery department performs approximately 500 neurosurgery and neuroendovascular operations each year.

All consecutive patients who underwent interventional therapy for cervical carotid artery stenosis in Nagoya University Hospital were enrolled in the present study. All patients were treated with CAS by using a balloon embolic protection device. Patients with stenoses related to radiation therapy or with restenoses after CEA were excluded from the present study.

The study was conducted in line with the requirements of the institutional review board. The authors obtained informed written consent from all individual subjects prior to the data collection. The CAS procedures and periprocedural management were in accordance with the institutional guidelines.

Definition of Terms

Any episodes of hypotension (defined as systolic blood pressure < or = 90 mm Hg), hypertension (defined as systolic blood pressure > 160 mm Hg), or bradycardia (defined as heart rate < 50 bpm) from the start of the interventional procedure to the fifth postprocedural day were recorded and defined as periprocedural hypotension, hypertension, or bradycardia, respectively. Patients who required continuous vasopressor infusion for more than three hours during and/or after the procedure were considered to have prolonged periprocedural hypotension.

Protocol for Carotid Artery Stenting Procedure

All procedures were performed under local anesthesia. Stenotic lesions with unstable and complex plaque were treated with proximal protection systems to avoid the risk of distal embolization by advancing the protection device through the stenosis [22]. The other lesions were treated with distal balloon protection. For prophylaxis intravenous atropine was given at a dose of either 0.25 mg (n = 3) or 0.5 mg (n = 45) before predilatation [8]. After predilatation, a self-expanding stent was deployed, followed by postdilatation.

Plaque Evaluation Using Virtual Histology

A VH IVUS was obtained before predilatation with the use of a VH IVUS console (Volcano Corporation). The total volume of each plaque type (fibrous, fibrofatty, dense calcium, and necrotic core) was calculated using VH IVUS software (version 1.3; Volcano Corporation) and expressed as cubic millimeters. The proportion of each plaque type was also determined.

Statistical Analysis

A univariate binary logistic regression analysis was performed to examine the effect of each variable on periprocedural hypotension or prolonged periprocedural hypotension. Multivariate stepwise logistic regression analysis was performed with entry criteria of $P < 0.20$.

We used the receiver operating characteristic (ROC) curve to quantify how well different scoring models could be used for the prediction of periprocedural hypotension and prolonged periprocedural hypotension [23]. Using a nonparametric method, we estimated the diagnostic accuracy of different scoring models by calculating the area under the ROC curve (ROC AUC). We also calculated the standard error (SE) and P value (null hypothesis, H0: AUC = 0.5; alternative hypothesis, H1: AUC > 0.5). The stratum specific likelihood ratios (SSLR) were

calculated with a method described by Peirce et Al.[23]. We used the logit method to calculate the 95% confidence intervals (CI) [23]. All statistical analyses were performed with the SPSS statistical software package (version 15.0; SPSS Inc, Chicago, IL).

Results

Fifty-four consecutive interventional therapies for cervical carotid artery stenosis in 50 patients were initially included in the present study. Since the VH analyses of the plaque were not available, six stenotic lesions (three stenotic lesions that had stenoses that were too severe for the VH IVUS catheter to cross before predilatation; three stenotic lesions in which the raw RF data captured in the VH IVUS console could not be recorded on a digital video disc because of technical difficulties) were also excluded. For the remaining 48 stenotic lesions in 45 patients, the descriptive characteristics are given in Table 1.

All the patients had successful dilatation of the carotid lesion by CAS. The mean degree of stenosis after the procedure was 3.3% (SD: 6.2; range: 0 to 20%). In the periprocedural period, no patients suffered from major adverse events, including symptomatic cerebral infarction, myocardial infarction or death. No patients needed repeated procedures or blood transfusions after the procedure. The mean degree of stenosis at the treated side was 74.0% (SD 14.8). The severity of stenosis ranged from 50% to 99% in all but 1 lesion (45% stenosis). In eight cases, the contralateral internal carotid artery (ICA) showed >50% stenoses (four cases had complete occlusion).

The authors performed 47 predilatation procedures. In 41 of these procedures a Submarine-Rapido balloon (INVAtec, Roncadelle, Italy) was used. An Amiia balloon (Johnson & Johnson, Miami, FL) was used in four cases. In two procedures a Savvy balloon (Johnson & Johnson) was used. In one case the stent was directly deployed and predilatation was unnecessary. Forty lesions were treated with a Precise stent (Johnson & Johnson). The other eight lesions were treated with a WallstentRP (Boston Scientific, Natick, MA). The authors also performed 42 postdilatation procedures. In 14 of these procedures a Submarine-Rapido balloon was used. In 28 procedures the authors used an Amiia balloon. In six cases no postdilatation was performed. The mean percentages for the plaque volumes in VH were as follows: 60.98% (SD 12.90) for fibrous tissue, 28.02% (SD 15.39) for fibrofatty tissue, 3.94% (SD 6.31) for dense calcium and 7.23% (SD 8.36) for necrotic core.

Univariate Influence of Characteristics

Periprocedural hypotension and prolonged periprocedural hypotension were observed in treating 36 of 48 (75%) lesions and in 29 of 48 (60%) lesions, respectively. The variables with a P value <0.20 (indicated in bold in Table 1) in the univariate analysis of periprocedural hypotension were: 1) history of diabetes mellitus (DM; risk of no history of DM > risk of history of DM); 2) distance between carotid bifurcation and minimum lumen site < or = 10 mm on angiogram; 3) stenotic lesion involving both the CCA and ICA on angiogram (vs. involving ICA only); 4) length of stent used (mm); 5) stent covering both the CCA and ICA (vs. covering ICA only); 6) length of predilatation balloon used (mm); 7) diameter of postdilatation balloon used (mm); 8) necrotic core (%) on VH and 8) fibrous tissue >60% on VH. The variables with a P value <0.20 (indicated in italics in Table 1) in the univariate analysis of prolonged periprocedural hypotension were: 1) sex (male risk > female risk); 2) distance between carotid bifurcation and minimum lumen site < or = 10 mm on angiogram; 3) stenotic lesion involving both the CCA and ICA on angiogram (vs. involving ICA only); 4) stent covering both the CCA and ICA (vs. covering ICA only); 5) type of postdilatation balloon used; 6) diameter of postdilatation balloon used and 7) carotid occlusion time (min). All of these variables indicated in either bold (periprocedural hypotension variables) or italics (prolonged periprocedural hypotension variables) were incorporated into the multivariate analyses.

Multivariate Analysis

Stepwise logistic regression analysis was used to derive the models for periprocedural hypotension and prolonged periprocedural hypotension. The final model for periprocedural hypotension consisted of the following independent variables: fibrous tissue >60% on VH, stenotic lesion involving both the CCA and ICA on angiogram, and no history of DM (Table 2). All three variables were significant independent risk factors for periprocedural hy-

potension. The P value of the Hosmer and Lemeshow's goodness-of-fit test (P = 0.998) and the Nagelkerke R-square value (R-square = 0.507) indicate a good fit of the model to the data.

For prolonged periprocedural hypotension, the final model consisted of the following independent variables: distance between carotid bifurcation and minimum lumen site < or = 10 mm on angiogram, and no history of DM (Table 2). The distance between carotid bifurcation and minimum lumen site < or = 10 mm on angiogram was a significant independent risk factor for prolonged periprocedural hypotension. The P value of the Hosmer and Lemeshow's goodness-of-fit test (P = 0.827) and the Nagelkerke R-square value (R-square = 0.315) indicate a good fit to the data.

There were no correlations between the factor of "distance between carotid bifurcation and minimum lumen site < or = 10 mm" and the factor of "fibrous tissue > 60% on VH" (Cramer's coefficients of association = 0.072) nor between the factor of "distance between carotid bifurcation and minimum lumen site < or =10 mm" and the factor of "no history of DM" (Cramer's coefficients of association = 0.195). The factor of "stenotic lesion involving both the CCA and ICA on angiogram" correlated weakly (Cramer's coefficient of association = 0.369) with the factor of "distance between carotid bifurcation and minimum lumen site < or = 10 mm on angiogram."

Carotid Morphologic Autonomic Pathologic Score

The four significant multivariate risk factors identified above can have 15 possible scoring models. Therefore, we calculate these 15 different scoring models with the four significant risk factors for periprocedural hypotension and/or prolonged periprocedural hypotension. Each scoring model presented different test results. We analyzed the diagnostic value of each scoring model with ROC AUC as shown in Figure 1. Of the 15 scoring models, the one which included all four significant risk factors (the "FSDN" model in Figure 1) performed the best discrimination with ROC AUC of 0.876 (SE 0.053, P < 0.001; for prediction of periprocedural hypotension) and 0.811 (SE 0.066, P< 0.001; for prediction of prolonged periprocedural hypotension). We defined this scoring model which included all four significant risk factors as the "carotid morphologic autonomic pathologic score (carotid MAPS)" (Table 3). The SSLRs of carotid MAPS with 95% CIs are shown in Table 4, demonstrating the discriminating power of the strata of the carotid MAPS.

Discussion

The present study has two novel findings. First, it shows that fibrous carotid plaque is a risk factor for periprocedural hypotension in CAS. Second, the carotid MAPS, which includes the findings that are related to plaque morphology, autonomic function and plaque pathology is clinically useful for predicting both periprocedural hypotension and prolonged periprocedural hypotension in CAS.

Risk Factors for Periprocedural Hypotension and Prolonged Periprocedural Hypotension

The present study confirmed that there are three risk factors of periprocedural hypotension and one risk factor of prolonged periprocedural hypotension in CAS (Table 2). The mean volume of fibrous tissue in this study was 60%. The factor of "fibrous tissue > 60% on VH" shows that fibrous tissue is composed of more than 60% of the whole plaque volume. In our study we detected that the factor of "fibrous tissue > 60% on VH" increased the risk of patients developing hypotension. Plaque that has more than 60% fibrous tissue content can be called fibrous plaque. Fibrous plaque is thought to create a hard surface in the circumference of the artery. As a result, carotid bulb baroreceptors of patients with fibrous plaque may be compressed directly and severely by dilatation balloons or stents. This may contribute to hypotension.

Our analysis has shown that patients who have lesions involving both the CCA and ICA are at higher risk of developing hypotension. This result is in agreement with the results of other studies [4,9] which reported that lesions involving the carotid bifurcation would predispose to the development of hypotension after CAS. Nonaka et Al.[11] reported, using univariate analysis, that the distance between carotid bifurcation and maximum stenotic lesion < or = 10 mm is a risk factor for the presence of prolonged hypotension. Our analysis has shown that the distance between carotid bifurcation and minimum lumen site < or = 10 mm

Table 1 **Association of hypotension with characteristics.**

	Periprocedural hypotension					Prolonged periprocedural hypotension				
Variables	**Yes (n =36)**		**No (n =12)**		**P value**	**Yes (n =29)**		**No (n =19)**		**P value**
Clinical characteristics										
Age (years old)	68.7	(SD 7.2)	68.9	(SD 6.8)	0.94	68.6	(SD 7.5)	69.1	(SD 6.5)	0.79
Female (vs. male)	4	(11%)	2	(17%)	0.62	1	(3%)	5	(26%)	*0.044*
History										
Hypertension	26	(72%)	7	(58%)	0.37	20	(69%)	13	(68%)	0.97
Diabetes mellitus	13	(36%)	7	(58%)	**0.18**	10	(34%)	10	(53%)	0.22
Hyperlipidemia	20	(56%)	8	(67%)	0.50	16	(55%)	12	(63%)	0.58
Beta blocker medication	2	(6%)	2	(17%)	0.25	2	(7%)	2	(11%)	0.66
Coronary artery disease	10	(28%)	5	(42%)	0.37	9	(31%)	6	(32%)	0.97
Myocardial infarction	5	(14%)	2	(17%)	0.81	5	(17%)	2	(11%)	0.52
Angina pectoris	9	(25%)	4	(33%)	0.58	8	(28%)	5	(26%)	0.93
Valvular heart disease	3	(8%)	1	(8%)	1.00	2	(7%)	2	(11%)	0.66
Arrhythmia	0	(0%)	1	(8%)	1.00	0	(0%)	1	(5%)	1.00
Congestive heart failure	2	(6%)	2	(17%)	0.25	2	(7%)	2	(11%)	0.6
Coronary artery bypass graft operation	1	(3%)	0	(0%)	1.00	1	(3%)	0	(0%)	1.00
Chronic renal insufficiency	1	(3%)	1	(8%)	0.43	1	(3%)	1	(5%)	0.76
Arteriosclerosis obliterans	3	(8%)	0	(0%)	1.00	2	(7%)	1	(5%)	0.82
Malignant neoplasm	2	(6%)	0	(0%)	1.00	2	(7%)	0	(0%)	1.00
Preprocedural systolic blood pressure (mm Hg)	118.5	(SD 17.2)	121.8	(SD 12.9)	0.55	118.4	(SD 17.7)	120.6	(SD 13.8)	0.65
Preprocedural diastolic blood pressure (mm Hg)	65.7	(SD 12.2)	67.5	(SD 10.2)	0.64	65.1	(SD 12.5)	67.7	(SD 10.3)	0.44
Periprocedural hypertension	5	(14%)	2	(17%)	0.81	3	(10%)	4	(21%)	0.31
Periprocedural bradycardia	5	(14%)	2	(17%)	0.81	4	(14%)	3	(16%)	0.85
Lesion-related characteristics										
Lesion side: left (vs. right)	18	(50%)	7	(58%)	0.62	16	(55%)	9	(47%)	0.60
Distance between carotid bifurcation and MLS < or = 10 mm (vs. > 10 mm)	30	(83%)	6	(50%)	**0.028**	26	(90%)	10	(53%)	*0.007*
Plaque ulceration deeper than 2 mm	15	(42%)	4	(33%)	0.61	12	(41%)	7	(37%)	0.75
Stenotic lesion involving both CCA & ICA (vs. ICA only)	18	(50%)	1	(8%)	**0.029**	15	(52%)	4	(21%)	*0.039*
Degree of treated stenosis (%)	73.3	(SD 14.9)	74.6	(SD 16.6)	0.80	73.7	(SD 14.8)	73.4	(SD 16.1)	0.95

	Periprocedural hypotension					Prolonged periprocedural hypotension				
Variables	**Yes (n =36)**		**No (n =12)**		**P value**	**Yes (n =29)**		**No (n =19)**		**P value**
Intracranial ICA stenosis, ipsilateral	4	(11%)	0	(0%)	1.00	2	(7%)	2	(11%)	0.66
Intracranial ICA stenosis, contralateral	2	(6%)	0	(0%)	1.00	2	(7%)	0	(0%)	1.00
Vertebrobasilar artery stenosis(>50%)	2	(6%)	0	(0%)	1.00	1	(3%)	1	(5%)	0.76
Contralateral ICA stenosis (>50%) or occlusion	6	(17%)	2	(17%)	1.00	6	(21%)	2	(11%)	0.36
Contralateral ICA occlusion	3	(8%)	1	(8%)	1.00	3	(10%)	1	(5%)	0.54
Symptomatic carotid stenosis, ipsilateral	17	(47%)	8	(67%)	0.25	13	(45%)	12	(63%)	0.22
Cerebral infarction, ipsilateral	12	(33%)	6	(50%)	0.31	9	(31%)	9	(47%)	0.26
Cerebral infarction, contralateral	6	(17%)	1	(8%)	0.49	3	(10%)	4	(21%)	0.31
Symptoms of carotid stenosis within 3 months, ipsilateral	7	(19%)	4	(33%)	0.33	5	(17%)	6	(32%)	0.25
Cerebral infarction within 3 months, ipsilateral	4	(11%)	3	(25%)	0.25	3	(10%)	4	(21%)	0.31
History of CAS or CEA, contralateral	5	(14%)	0	(0%)	1.00	4	(14%)	1	(5%)	0.36
Treatment-related characteristics										
Stent used: Wallstent RP (vs. Precise Stent)	7	(19%)	1	(8%)	0.39	5	(17%)	3	(16%)	0.90
Stent diameter (mm)	9.8	(SD 0.4)	9.6	(SD 1.1)	0.41	9.8	(SD 0.4)	9.7	(SD 0.9)	0.71
Stent length (mm)	33.2	(SD 8.1)	37.0	(SD 5.4)	**0.15**	33.9	(SD 8.1)	34.4	(SD 7.1)	0.83
Stent covering both CCA & ICA (vs. ICA only)	33	(92%)	9	(75%)	**0.15**	27	(93%)	15	(79%)	*0.17*
Predilatation										
Balloon catheter used (vs. Submarine)										
Amiia	3	(8%)	1	(8%)	0.98	3	(10%)	1	(5%)	0.53
Savvy	1	(3%)	1	(8%)	0.44	1	(3%)	1	(5%)	0.81
No predilatation	1	(3%)	0	(0%)	1.00	1	(3%)	0	(0%)	1.00
Balloon diameter (mm)	3.7	(SD 0.8)	4.0	(SD 0.7)	0.34	3.7	(SD 0.8)	4.0	(SD 0.6)	0.23
Balloon length (mm)	29.2	(SD 7.6)	34.2	(SD 6.4)	**0.050**	29.3	(SD 8.3)	32.1	(SD 6.1)	0.23
Balloon inflation pressure (atm)	7.4	(SD 2.0)	7.8	(SD 1.3)	0.48	7.3	(SD 2.0)	7.8	(SD 1.5)	0.35

	Periprocedural hypotension					Prolonged periprocedural hypotension				
Variables	**Yes (n =36)**		**No (n =12)**		**P value**	**Yes (n =29)**		**No (n =19)**		**P value**
Balloon inflation duration (sec)	33.4	(SD 12.3)	31.3	(SD 9.6)	0.58	33.1	(SD 12.5)	32.5	(SD 10.3)	0.86
Postdilatation										
Balloon catheter used (vs. Submarine)										
Amiia	22	(61%)	6	(50%)	1.00	19	(66%)	9	(47%)	*0.13*
No postdilatation	3	(8%)	3	(25%)	0.21	2	(7%)	4	(21%)	0.34
Balloon diameter (mm)	4.9	(SD 1.6)	4.1	(SD 2.4)	**0.20**	5.1	(SD 1.5)	4.1	(SD 2.2)	*0.10*
Balloon length (mm)	20.1	(SD 7.9)	18.3	(SD 11.4)	0.55	20.5	(SD 7.8)	18.4	(SD 10.4)	0.44
Balloon inflation pressure (atm)	10.2	(SD 3.7)	8.5	(SD 5.2)	0.24	10.3	(SD 3.5)	8.9	(SD 5.0)	0.28
Emboli-protection method: proximal protection (vs. distal protection)	1	(3%)	4	(33%)	0.79	2	(7%)	3	(16%)	0.98
Occlusion time (min)	11.0	(SD 4.68)	11.6	(SD 2.81)	0.68	11.6	(SD 4.70)	10.4	(SD 3.45)	*0.14*
Virtual Histology findings of plaque volumetric composition analysis										
Fibrous tissue (%)	62.0	(SD 12.4)	57.9	(SD 13.4)	0.35	61.8	(SD 13.4)	59.7	(SD 11.5)	0.59
Fibrofatty tissue (%)	28.6	(SD 15.3)	26.2	(SD 14.8)	0.63	29.0	(SD 16.8)	26.6	(SD 12.3)	0.60
Dense calcium (%)	3.2	(SD 3.2)	6.1	(SD 10.9)	0.24	3.1	(SD 3.2)	5.2	(SD 8.9)	0.33
Necrotic core (%)	6.3	(SD 7.0)	10.1	(SD 10.8)	**0.19**	6.2	(SD 7.4)	8.8	(SD 9.2)	0.31
Dichotomous variables (dichotomized at mean)										
Fibrous tissue > 60%	21	(58%)	4	(33%)	**0.14**	17	(59%)	8	(42%)	0.27
Fibrofatty tissue > 28%	14	(39%)	6	(50%)	0.50	11	(38%)	9	(47%)	0.52
Dense calcium > 3%	13	(36%)	4	(33%)	0.86	11	(38%)	6	(32%)	0.65
Necrotic core > 7%	13	(36%)	5	(42%)	0.73	9	(31%)	9	(47%)	0.26

Variables with a P value <0.20 for periprocedural hypotension (indicated in bold) and prolonged periprocedural hypotension (indicated in italics) were incorporated into the multivariate analyses.
P values were derived from the univariate binary logistic regression. Continuous data are shown as the mean (SD).
Categorical data are shown as counts (%). MLS = minimum lumen site; CAS = carotid artery stenting;
CEA = carotid endarterectomy.

is an independent risk factor of prolonged periprocedural hypotension. We obtained this result by using multivariate analysis. These risk factors cause periprocedural hypotension or prolonged hypotension probably because of the higher concentration of baroreceptors at this location.

Diabetes mellitus was found to be an independent variable that reduces the risk of patients developing hypotension. This result is in

Table 2 **Determinants of hypotension derived from multivariate logistic regression.**

Variables	Coefficient	SE	Wald	P value	OR (95% CI)	
Periprocedural hypotension						
Fibrous tissue > 60% on Virtual Histology (vs. < or = 60%)	2.54	1.16	4.78	0.029	12.69	(1.30 to 124)
Stenotic lesion involving both CCA and ICA on angiogram (vs. ICA only)	4.59	1.59	8.33	0.004	98.38	(4.36 to 2220)
No history of diabetes mellitus	2.81	1.21	5.40	0.020	16.60	(1.55 to 178)
Constant	-2.69	1.28	4.45	0.035		
Prolonged periprocedural hypotension						
Distance between carotid bifurcation and MLS < or = 10 mm on angiogram (vs. > 10 mm)	2.61	0.88	8.75	0.003	13.66	(2.42 to 77.2)
No history of diabetes mellitus	1.49	0.76	3.82	0.051	4.45	(1.00 to 19.9)
Constant	-2.32	0.96	5.84	0.016		

SE = standard error; Wald = Wald statistic; OR = odds ratio; CI = confidence interval; MLS = minimum lumen site.

agreement with the findings of another study [4] that demonstrated that patients with DM are protected from hypotension. Autonomic function is impaired in patients with DM [24]. This may be the reason patients with DM have an impaired ability to develop hypotension during balloon inflation and stent deployment.

As described above, the risk factors which we identified are in agreement with the findings of earlier studies by other authors. In addition, we identified fibrous carotid plaque as a novel risk factor of periprocedural hypotension in CAS. This is the first demonstration of the correlation between the findings of Virtual His-

Table 3 **Carotid Morphologic Autonomic Pathologic Score**

Modality	Factor	Point
Morphology (Angiography)	Distance between carotid bifurcation and MLS < or = 10 mm Distance between carotid bifurcation and MLS > 10 mm	1 0
Morphology (Angiography)	Stenotic lesion involving both CCA and ICA Stenotic lesion involving ICA	1 0
Autonomic function (Patient's characteristic)	No history of diabetes mellitus History of diabetes mellitus	1 0
Pathology (Virtual Histology)	Fibrous tissue > 60% Fibrous tissue < or = 60%	1 0
	Total	0 to 4

MLS = minimum lumen site.

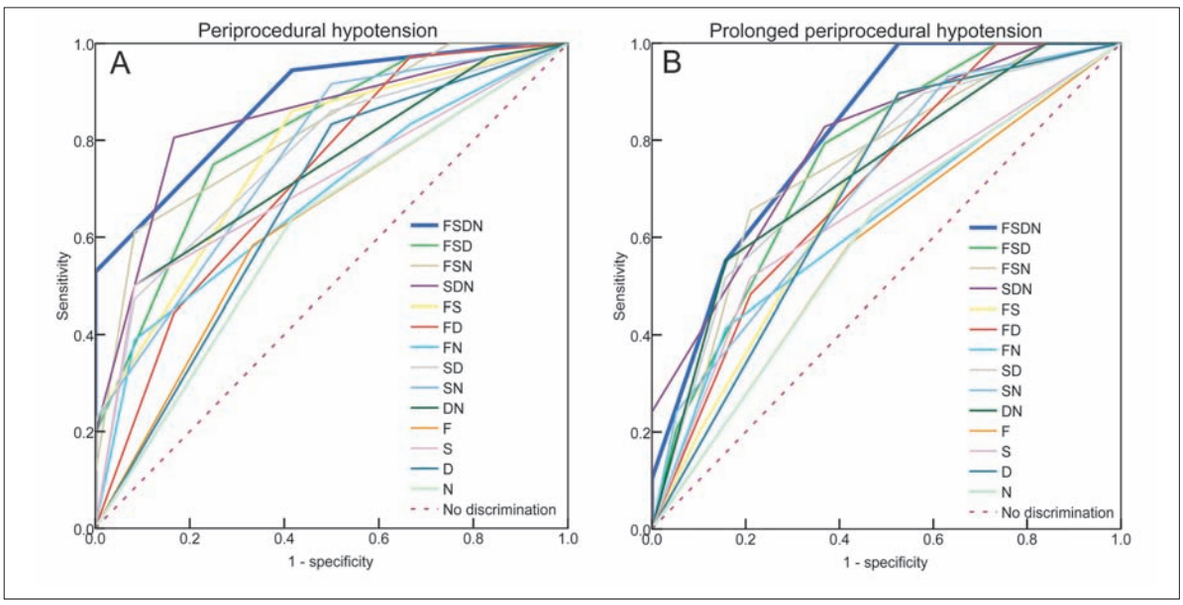

Figure 1 The receiver operating characteristic curves of all 15 scoring models showing the diagnostic value of each scoring model for the prediction of periprocedural hypotension (A) and prolonged periprocedural hypotension. All 15 scoring models are based on the four significant multivariate risk factors for periprocedural hypotension and/or prolonged periprocedural hypotension. The best discrimination was achieved by carotid MAPS (carotid morphologic autonomic pathologic score; the model "FSDN"). F = fibrous tissue > 60% on Virtual Histology; S = stenotic lesion involving both the common carotid artery and internal carotid artery on angiogram; D = distance between carotid bifurcation and minimum lumen site < or = 10 mm on angiogram; N = no history of diabetes mellitus.

Table 4 **Strata of carotid morphologic autonomic pathologic score and stratum specific likelihood ratios.**

	No of patients				**Likelihood ratio**		
Carotid MAPS	**Yes**	**No**	**Sensitivity**	**Specificity**	**(95% CI)**		**Probability**
Hypotension							
4	3	0	0.08	1.00	> 999		1.00
3	16	0	0.53	1.00	> 999		1.00
2	15	5	0.94	0.58	1.00	(0.48 to 2.08)	0.75
1	2	6	1.00	0.08	0.11	(0.03 to 0.41)	0.25
0	0	1	1.00	0.00	0.00	(0.00 to 0.00)	0.00
Prolonged hypotension							
4	3	0	0.10	1.00	> 999	1.00	
3	13	3	0.55	0.84	2.84	(1.02 to 7.93)	0.81
2	13	7	1.00	0.47	1.22	(0.61 to 2.41)	0.65
1	0	8	1.00	0.05	0.00	(0.00 to 0.00)	0.00
0	0	1	1.00	0.00	0.00	(0.00 to 0.00)	0.00

Carotid MAPS = carotid morphologic autonomic pathologic score

tology and periprocedural clinical course in patients undergoing neurointerventions. The result of the present study indicates the usefulness of plaque evaluation with the use of VH IVUS in neurointerventions as well as coronary interventions.

Clinical Usefulness of the Carotid Morphologic Autonomic Pathologic Score

The carotid MAPS is clinically useful for predicting both periprocedural hypotension and prolonged periprocedural hypotension in CAS. Periprocedural hypotension and prolonged hypotension, which often occur in CAS [2-6,11], are important risk factors for complications such as stroke or death after CAS [3,4]. Predicting periprocedural hypotension and prolonged hypotension may be important for preventing complications in CAS. In addition, identification of patients at high risk has gained more importance because of the possibility of same-day discharge for some of these patients [25].

We propose the use of carotid MAPS, which includes the findings that are related to plaque morphology (angiography), autonomic function (history of DM), and plaque pathology (Virtual Histology). We evaluated the 15 different scoring models based on the four significant multivariate risk factors (Figure 1). As a result, the carotid MAPS (Table 3) was determined to be the best. The carotid MAPS can significantly predict both hypotension ($P < 0.001$) and prolonged hypotension ($P < 0.001$) in CAS.

We evaluated the SSLRs of carotid MAPS (Table 4) for clinical use. With the use of SSLRs, carotid MAPS is generalizable to the CAS procedures with the wide variation in prevalence of periprocedural hypotension in various hospitals. According to Bayes' theorem, the probability of the presence of the event (periprocedural hypotension or prolonged periprocedural hypotension) is calculated with the formula:

$$PROB = SSLR / (SSLR - 1 + 1 / PREV)$$

where:
PROB = the probability of the presence of the event in CAS
SSLR = the likelihood ratio of the carotid MAPS of the patient
PREV = the prevalence of the event in a given hospital

For example, the prevalence (PREV) of prolonged hypotension in our hospital is 0.60. For a patient with a carotid MAPS 3, the likelihood ratio (SSLR) is 2.84 for prolonged hypotension. Therefore, the probability (PROB) of the presence of prolonged hypotension is calculated as 0.81, i.e. the probability that the patient suffers from prolonged hypotension after CAS will be 81%. Note that the prevalence (PREV) of hypotension or prolonged hypotension differs from one hospital to another. By contrast SSLRs are universal because each scoring model has fixed sets of sensitivity and specificity. However, the probability of the presence of the event (the positive predictive value) depends upon the prevalence of the event in a given population. As described above, the carotid MAPS can predict both periprocedural hypotension and prolonged periprocedural hypotension. In addition, with the use of SSLRs, carotid MAPS is generalizable to the CAS procedures in other hospitals. In light of these results, carotid MAPS will be clinically useful for predicting both periprocedural hypotension and prolonged periprocedural hypotension in CAS.

Limitations of the Present Study

There are some weaknesses in our study. The first is that the number of patients in the present study is relatively small. The series of 48 CAS procedures in 45 patients had sufficient power for the construction of the good-fit multivariate logistic regression models. However, a larger series may help to identify better-fit multivariate models with a more accurate and simpler scoring model. The second weakness is that the present study was performed in a single center. Although SSLRs can be applied to other hospitals, it is more complicated to calculate the probabilities of the presence of hypotension and prolonged hypotension with the use of SSLRs. After a consensus is reached on periprocedural management and CAS procedures, the wide variation of the prevalence of hypotension among the hospitals will decrease. The third is that the carotid MAPS should also be evaluated with use of a test set. We are conducting an ongoing prospective clinical study to describe the discrimination ability of the carotid MAPS. The forth is that a VH IVUS catheter has a short detection range (10 mm in diameter). We were able to evaluate the plaque only within the de-

tection range. The development of new VH IVUS catheters with longer range is needed for the more accurate evaluation of carotid plaque. The fifth is that it is unclear whether pre-treating high-risk patients aggressively may prevent hypotension or prolonged hypotension, and subsequently reduce the risk of adverse vascular events. Further investigation is required with respect to the effects of predicting hypotension on the prognoses of these patients. The results of the present study may contribute to the improvement in prognosis and comfort of patients undergoing CAS. Identifying the patients at high risk of periprocedural hypotension will enable them to receive stricter periprocedural management that may result in further improvement in patient prognosis in CAS. Moreover, the results of the present study may allow patients at low risk of periprocedural hypotension to undergo ambulatory CAS. Consequently, this will enhance the applicability of CAS by increasing patient comfort and potentially reducing procedural costs.

Conclusions

The results of the present study indicate the possible use of the carotid MAPS in discriminating patients at high or low risk of periprocedural hypotension and prolonged periprocedural hypotension in CAS.

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Shigeru Miyachi, M.D.
Department of Neurosurgery
Nagoya University
Graduate School of Medicine,
65 Tsurumaicho, Showaku
Nagoya 466-8550, Japan.
E-mail: smiyachi@med.nagoya-u.ac.jp