

Optimizing the Volume of the Initial Framing Coil to Facilitate Tight Packing of Intracranial Aneurysms

著者	Misaki Kouichi, Uchiyama Naoyuki, Nambu Iku, Aida Yasuhiro, Kamide Tomoya, Mohri Masanao, Ueda Fumiaki, Nakada Mitsutoshi
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Optimizing the volume of the initial framing coil to facilitate tight packing of intracranial aneurysms

Kouichi Misaki, MD^a, Naoyuki Uchiyama, MD^a, Iku Nambu, MD^a, Yasuhiro Aida, MD^a, Tomoya Kamide, MD^a, Masanao Mohri, MD^a, Fumiaki Ueda, MD^b, Mitsutoshi Nakada, MD^a *Kanazawa, Japan*

From the Department of Neurosurgery, Division of Neuroscience^a, and Department of Radiology, Division of Cardiovascular Medicine^b, Graduate School of Medical Science, Kanazawa University, Japan

Corresponding author: Kouichi Misaki

Department of Neurosurgery, Division of Neuroscience, Graduate School of Medical Science, Kanazawa University, 13-1 Takara-machi, Kanazawa, Ishikawa 920-8641, Japan

Phone: +81-76-265-2384, Fax: +81-76-234-4262

E-mail: misaki@med.kanazawa-u.ac.jp

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Abbreviation list: ICA; internal carotid artery, PD; packing density, ROC; receiver operating characteristic

ABSTRACT

Background: During endovascular treatment of an aneurysm, the importance of the initial coil volume for facilitating tight packing is unclear. We retrospectively studied the relationships between initial packing density (PD; initial coil volume divided by aneurysm volume), final PD (volume of all coils divided by aneurysm volume).

Methods: We reviewed 105 aneurysms in 98 patients who underwent endovascular coiling between April 2011 and March 2014. The initial coil was defined as the first coil in the single-catheter method and the first two coils in the double-catheter method. The patient data were divided into groups with or without a final PD $\geq 20\%$, and the significant predictors of a final PD $\geq 20\%$ were determined using multivariable logistic regression. The optimal cutoff value for the initial PD was determined using a receiver operating characteristic (ROC) curve.

Results: Among 105 aneurysms, 56 and 49 were treated with single- and double-catheter methods, respectively. Statistically significant differences in rupture status, neck size, dome-to-neck ratio, and initial PD were observed between aneurysms with and without a final PD $\geq 20\%$ (all $p < 0.05$). Multivariate analysis showed that initial PD ($p = 0.025$; OR, 1.22) and rupture status ($p = 0.002$; OR, 0.19) were significantly associated with a final PD $\geq 20\%$. Using ROC curve analysis, the cutoff points of initial PD to achieve a final PD $\geq 20\%$ were 8.0% and 10.0% in single- and double-catheter groups, respectively.

Conclusion: Initial PD appears to be a critical factor for achieving tight packing.

Introduction

Endovascular treatment of cerebral aneurysms with detachable coils has proven to be a safe and effective alternative to surgical clipping.¹ However, a limitation of endovascular coiling is its increased risk for aneurysm recurrence compared with surgery.^{1, 2} Multiple retrospective studies have shown an inverse relationship between aneurysm recurrence and coil packing density (PD), which is the percentage of the aneurysm volume occupied by the coils.³⁻⁸ The necessity of tight packing for the prevention of aneurysm recurrence has been stressed; several authors have reported that aneurysm recurrence occurred in cases with a PD smaller than 20%.^{4, 7, 9-11} Although stable framing with the first coil is thought to be important for achieving a tight final PD, limited data exist regarding the selection criteria for the first framing coil used in endovascular treatment. In cases of wide neck aneurysm, there is a greater need for stable framing to prevent migration of additional coils into the parent artery, whereas a framing coil also has a tendency to herniate into the parent artery during insertion. To prevent migration of initial coils into the parent artery in wide neck aneurysms, the double-catheter method is widely used to provide strong framing, and to enable the choice of the two optimal coils before detachment.³ We defined initial PD as the first coil alone in the single-catheter method and the first two coils in the double-catheter method, and retrospectively studied the importance of the initial PD in prediction of the final PD. We hypothesized that the initial PD would influence the final PD and we aimed to identify a cutoff value associated with an improved outcome.

Materials and Methods

Database

Between April 2011 and March 2014, we treated 156 intracranial aneurysms using coil embolization at our hospital. For the present study, we excluded 51 aneurysms because they were treated with parent artery occlusion with coil (18), were retreatment procedures (17), or involved stent-assisted coiling (16). The

remaining 105 aneurysms in 98 patients were studied. The patient sample included 27 men and 71 women ranging in age from 30 to 91 years (mean, 60.6 years). The aneurysms consisted of 55 ruptured and 50 unruptured aneurysms. Eighty-one aneurysms were located in the anterior circulation and 24 in the posterior circulation. The specific locations were as follows: 26 at the internal carotid artery (ICA)–posterior communicating artery junction, 22 at the anterior communicating artery, 13 at the ICA–superior hypophyseal artery junction, 12 at the basilar tip, 9 at the middle cerebral artery, 6 at the basilar artery–superior cerebellar artery junction, 5 at the ICA–anterior choroidal artery junction, 4 at the vertebral artery–posterior inferior cerebellar artery junction, 3 at the distal anterior cerebral artery, and 1 at each of the proximal anterior cerebral artery, ICA–ophthalmic artery junction, ICA bifurcation, posterior cerebral artery, and basilar artery–anterior inferior cerebellar artery junction.

Aneurysm volume was measured using a partially automated 3-dimensional workstation (Allura 3D-RA workstation, Philips Medical Systems) from rotational angiography data.¹² The volume of the coils was defined as $\pi (p/2)^2$ times coil length, where p is the primary coil diameter. The initial PD was obtained by dividing the first coil volume by the aneurysm volume and the final PD by dividing the volume of all inserted coils by the aneurysm volume.

Endovascular treatment and follow-up

Endovascular treatment was performed within 72 hours of the primary hemorrhage in cases of aneurysm rupture. Patients with unruptured aneurysms were pretreated with aspirin and clopidogrel in preparation for treatment. Coil embolization was performed via the transfemoral approach under general anesthesia. Intravenous heparin was given systemically in all cases. The double-catheter method was selected in cases with a wide neck (≥ 4 mm) or tendency for the initial coils to herniate into the parent artery. We used double-catheter method and assist balloons during the embolization procedure for 49 and 19 aneurysms, respectively. The diameter of the initial coil was determined as the mean size of the maximum diameter and

height of the aneurysm or equal to its height, and the longest passable coil in this selection was inserted as the initial coil. The first coil inserted in the aneurysm was a Target coil (Stryker, Kalamazoo, MI, USA) in 46 aneurysms, Cashmere coil (Johnson & Johnson, Miami, FL, USA) in 40 aneurysms, GDC 18 coil (Stryker, Kalamazoo, MI, USA) in 6 aneurysms, Presidio (Johnson & Johnson, Miami, FL, USA) in 6 aneurysms, and other types in the remaining 6 aneurysms. GDC 18 and Presidio coils were selected as the first coil in cases with large (≥ 10 mm) aneurysms, whereas Target and Cashmere coils were selected for small aneurysms. In all cases, the Target coils were 360 coils, except for 4 aneurysms in which helical coils were used as the initial coil. Subsequent coils were inserted until the aneurysm was excluded from the circulation or until no more coils could be delivered. All aneurysms were packed with bare platinum coils except for 4 aneurysms that were treated using Hydrosoft coils (Terumo, Tokyo, Japan).

We obtained postembolization follow-up gadolinium-enhanced time-of-flight images at 3, 6, and 12 months and yearly thereafter to define any residual lesions. When these images indicated increasing residual lesions, we performed cerebral angiography. We defined aneurysm recurrence as cases with major coil compaction that required retreatment because of a risk of bleeding¹³. The mean follow-up interval was 28.6 months (range, 11–48).

Data analysis

We collected the following information from the hospital records of each eligible patient: demographic information including age, sex, and rupture status; angiographic data detailing the aneurysm characteristics including the maximum dome size, neck size, dome-to-neck ratio, and volume; data describing the endovascular procedure techniques such as a balloon neck plasty or the use of double-catheters; the type of first coil inserted; the initial and final PD; the immediate angiographic occlusion type (complete occlusion, neck remnant, or body filling); and aneurysm recurrence.

A final PD $\geq 20\%$ was considered a favorable outcome in this study. This level was chosen because

several reports have demonstrated that the requisite final PD for aneurysm stability is 20%.^{4,7,9-11} One report that considered the size of the aneurysm also demonstrated that a final PD of 20% was associated with stability in aneurysms with a volume less than 200 mm³, and a final PD of 24% was needed for stability in aneurysms with a volume greater than 600 mm³.^{3,5} Another report assessed the optimal final PD according to aneurysm status, and found that the optimal final PD for aneurysm stability in ruptured and unruptured aneurysms was 30% and 20%, respectively.⁹ In this study, the patient data were divided into groups with or without a final PD \geq 20% because previously published data, which included both small and large aneurysms and both ruptured and unruptured aneurysms, have shown this to be a clinically relevant distinction.

All statistical analyses were performed using IBM SPSS Statistics, version 19.0 (SPSS, Inc., Chicago, IL, USA). The chi-squared test was used for categorical variables and the nonparametric Mann–Whitney test for quantitative variables to determine the associations between patient characteristics and a final PD \geq 20%. The most significant predictors of a final PD \geq 20% were determined using multivariable logistic regression analysis. We used a receiver operating characteristic (ROC) curve analysis to determine the optimal cutoff value of the initial PD that optimizes a final PD \geq 20%. All aneurysms were subdivided into 2 groups on the basis of this cutoff value, and we used a chi-squared test to assess the relationship between initial PD and immediate angiographic occlusion and aneurysm recurrence. Statistical tests were conducted at the $p < 0.05$ significance level. This study has been approved by the appropriate ethics committee and has therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.

Results

The 105 aneurysms had a maximum dome size of 7.5 ± 3.2 mm (mean \pm standard deviation), neck size of 4.2 ± 1.9 mm, dome-to-neck ratio of 1.9 ± 0.9 , and aneurysm volume of 244 ± 414 mm³. The mean final PD was $22.7\% \pm 6.3\%$ and initial PD was $10.4\% \pm 5.2\%$ (Table 1). Among the demographic factors, rupture status,

neck size, dome-to-neck ratio, and initial PD were associated with a final PD $\geq 20\%$ in the univariate analyses (Table 1). The percentage of ruptured aneurysms in patients who had a PD $\geq 20\%$ was significantly lower than in those with PD $< 20\%$ (44% vs. 72%, $p = 0.011$). The mean neck size of aneurysms with a final PD $\geq 20\%$ was smaller than that of aneurysms with a PD $< 20\%$ (3.7 ± 1.3 mm vs. 5.2 ± 2.6 mm, $p = 0.002$). The average dome-to-neck ratio and initial PD were significantly larger for aneurysms with a final PD $\geq 20\%$ than those with a PD under 20% (2.0 ± 0.6 vs. 1.8 ± 1.3 , $p = 0.022$; and $11.5\% \pm 5.3\%$ vs. $7.8\% \pm 4.1\%$, $p < 0.001$, respectively). There was no significant relationship between the final PD and kind of the first coil. The intraoperative rupture of aneurysm occurred in two cases during insertion of filling coil which was arrested by additional coil insertion without neurological deterioration. There was no intraoperative rupture during insertion of the initial coil.

Among the significant factors (rupture status, neck size, dome-to-neck ratio, and initial PD) from the univariate analyses, multivariable logistic regression analysis showed a significant relationship between final PD $\geq 20\%$ and initial PD ($p = 0.025$; OR, 1.22; 95% CI, 1.03–1.45) and rupture status ($p = 0.002$; OR, 0.19; 95% CI, 0.07–0.55) (Table 2).

Single- and double-catheter methods were selected in 49 and 56 aneurysms, respectively. The morphological factors that showed a significant difference among single- and double-catheter groups were the maximum dome size, neck size, and aneurysm volume (all $p < 0.05$, Table 3). There was no significant difference in dome to neck ratio and initial PD among single- and double-catheter method groups, whereas the PD of the first coil (9.9 ± 5.0 vs. 7.1 ± 4.4 , $p < 0.001$) and the final PD (24.2 ± 7.1 vs. 20.9 ± 4.7 , $p = 0.005$) were significantly greater in the single-catheter group than in the double-catheter group (Table 3).

The ROC curve analysis confirmed an association between initial and final PD $\geq 20\%$, with an area under the curve of 0.808 ($p = 0.001$; 95% CI, 0.687–0.929) and 0.702 ($p = 0.018$; 95% CI, 0.541–0.862) in single- and double-catheter groups, respectively (Fig. 1). With an initial PD cutoff point of 8.0% in the single-catheter group, the sensitivity and specificity were 76.7% and 69.2%, respectively (Fig. 1). In the

double-catheter group, a cutoff point of 10.0% for the initial PD resulted in a sensitivity and specificity of 76.7% and 63.2%, respectively (Fig. 1). On the basis of the ROC curve analysis, we subdivided the 105 aneurysms into 2 groups: 67 aneurysms with an initial PD over the cutoff value (favorable initial PD) and 38 under the cutoff value. A final PD $\geq 20\%$ was observed in 56/67 (83%) aneurysms with a favorable initial PD, and in 17/38 (45%) aneurysms without a favorable initial PD; scatter plot data that demonstrate the relationship among final PD and maximum dome diameter in aneurysms with and without favorable initial PD in single- and double-catheter groups are shown in figure 2.

Within the mean follow-up period of 28.6 months (range, 11–48), major recurrence with retreatment was observed in 11 (11%) of the 105 aneurysms. Compared with those with a high final PD, i.e., PD $\geq 20\%$, the less-packed aneurysms (PD $< 20\%$) had a higher incidence of recurrence (6% vs. 22%, $p = 0.032$) (Table 1). Additionally, the major recurrence rate was significantly higher for aneurysms without a favorable initial PD (18%) than an initial PD of under the cutoff value (6%, $p = 0.045$) (Table 4).

Discussion

This study is the first to advocate an initial PD of the cutoff values of 8.0% in the single-catheter method and 10.0% in the double-catheter method, as a standard framing coil volume to achieve tight packing of intracranial aneurysms. Construction of a stable frame by the initial coil enables the easy insertion of subsequent coils, without migration into the parent artery, and leads to a high final PD. This study found that 83% of cases with a favorable initial PD attained a final PD of 20%, whereas only 45% of cases without a favorable initial PD attained a final PD of 20% (Table 4). This result demonstrates that an initial PD of more than the cutoff values is required for tight coil packing.

This study recommends the selection of coils that are as long and as thick as possible, whereas the coils currently sold tend to be short with small diameters. In the cases of aneurysms with a low height and

wide neck, we occasionally could not choose long enough coils, because coils with a small diameter, which have short coil lengths, were selected to prevent coil migration into the parent artery due to the low height of the aneurysm.¹⁴ In this situation, the double-catheter method is useful because the addition of a second coil increases the strength of the framing coil basket, and careful selection of the two optimal coils is possible before coil detachment. This study shows that the double-catheter method was preferred in aneurysms with a significantly larger dome, neck, and volume compared with the single-catheter method, whereas there was no significant difference in the initial PD between the single- and double-catheter groups (Table 3). The PD of only the first coil was significantly smaller in the double catheter group than in the single catheter group (Table 3), and ROC analyses showed 8.0% to be the optimal point of initial PD (first coil) for favorable final PD, whereas the cutoff point of PD with the first coil only in the double catheter group was 5.7% ($p=0.008$; sensitivity and specificity: 0.867 and 0.632, respectively; data not shown). Although analysis of the first coil only in the double catheter group also showed significant results and is a simple study design, an indication of the first two coils for final dense packing has clinical importance because the first two coils can be chosen before detachment. This report shows that 10.0% of the PD from the first two coils (initial PD) provides a stable flaming to achieve dense final packing in the double catheter group containing a wide neck and large aneurysms. In addition to the double-catheter method, balloon remodeling and/or stent-assisted techniques are required during the endovascular treatment for wide neck and large aneurysms.¹⁴ The maximum ostium angle was reported to be a useful parameter for predicting the need for stent-assisted coiling in sidewall aneurysms.¹⁵ Similarly, the inability to achieve a favorable initial PD with the initial coil may be an indication to use these adjunctive techniques.

The theory that the coil selected should be as long and as thick as possible may result in intraoperative rupture of the aneurysm during insertion of the first coil. In this study, the diameter of the first coil was determined as the mean size of the maximum diameter and height of the aneurysm or equal to its height, and a primary coil with a width greater than 0.010 inch was chosen for an aneurysm with a maximum

diameter of >7 mm. The longest possible coil in this selection was inserted as the first coil, and there was no intraoperative rupture of an aneurysm during the first coil insertion.

Two morphological factors, neck size and dome-to-neck ratio, were significantly associated with a final PD $\geq 20\%$ in the univariate analysis. In contrast, these factors did not show a significant association in the multivariate analysis. These results demonstrate that the insertion of a long first coil is more important for tight packing than morphological factors. Although several reports have shown that factors associated with failed tight packing in endovascular treatment include a wide neck and large volume of the aneurysm, no reports considered the impact of the first coil volume in detail.⁴⁻⁸

In this study, ruptured aneurysms had a lower final PD than unruptured aneurysms: 58% (32/55) of ruptured and 82% (41/50) of unruptured aneurysms had a final PD $\geq 20\%$. In ruptured aneurysms, activation of systemic coagulation and platelet aggregation, which leads to intra-aneurysmal thrombus formation, occurs in the earlier stages of coil embolization.¹⁶ After the insertion of the first framing coil, we added coils until the contrast-medium-darkened aneurysm could no longer be observed. If the aneurysm was no longer observed without sufficient coil insertion because of activated thrombogenicity, no further coils were inserted in order to avoid intra-procedural rupture. In coil embolization of ruptured aneurysms, the coil insertion tends to be slower than that in unruptured aneurysms, which results in insufficient coil expansion and scanty coil packing. We believe that activated thrombus formation and restrained coil insertion are the reasons why ruptured aneurysms had a significantly lower final PD.

The factors reported to be related to aneurysm recurrence include aneurysm size, neck size, initial angiographic results, rupture status, and insufficient coil packing.^{3-5, 10, 13, 16} In this study, the initial PD, as well as the final PD, was significantly associated with aneurysm recurrence requiring retreatment. Although the correlation between the initial PD and aneurysm recurrence was marginal ($p = 0.045$), it is a remarkable finding that the final packing degree and subsequent recurrence could be predicted in the early stage by the first coil insertion during endovascular embolization.

This study had several limitations. The first limitation is the small sample size. Second, the PD was an indicator of coil volume relative to the whole aneurysm volume and did not represent coil distribution. In the cases with coil compartmentation and partial tight packing, these factors may influence the final PD and subsequent recurrence.^{17 18} Third, we did not evaluate the properties of the first coil inserted. Regarding coil configuration, we selected a 2-dimensional helical coil in only 4 aneurysms and coils with 3-dimensional configuration (Target 360, Cashmere, GDC-18 360, and Presidio) in most other aneurysms and a report shows utility of 3-dimensional coils over 2-dimensional coils for tight packing.¹⁹ We did not include the rigidity of the inserted coils in our analyses. Fourth, we included both unruptured and ruptured cases. To avoid intraoperative rupture of an aneurysm, coil selection and strategy partly differentiate between these two types of cases. Further investigation of the rupture status was needed, but this could not be done because of the small number of cases. Finally, this study was conducted in a retrospective fashion. Thus, inevitable selection bias exists. Further prospective studies with a large number of subjects are needed.

Conclusions

The results of our study indicate that the initial PD is associated with the tight final packing of intracranial aneurysms. This study also found that a cutoff value for the initial PD of 8.0% in single-catheter method and 10.0% in double-catheter method provide good specificity. The selection of the initial coil appears to determine the completeness of coil-embolized cerebral aneurysms.

Conflict of interest

We declare that we have no conflict of interest.

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Figure legends

Fig. 1 Receiver operating characteristic curve analysis to determine the optimal cutoff value to achieve a final packing density $\geq 20\%$

a: The cutoff value for the initial packing density was 8.0% in the single-catheter method, yielding optimal sensitivity and specificity (76.7% and 69.2%, respectively).

b: In the double-catheter method, the cutoff value was 10.0%, with optimal sensitivity and specificity (76.7% and 63.2%, respectively).

Fig. 2 Scatter plot depicting the relationship between final packing density and maximum dome diameter in aneurysms with (closed squares) or without (open diamonds) a favorable packing density, in single-catheter (a), and double-catheter (b) groups.

Table 1 Clinical characteristics of the aneurysms

	All aneurysms n = 105 (%)	Final PD \geq 20% n = 73 (%)	Final PD <20% n = 32 (%)	<i>P</i> value
Age (year)	61 \pm 14	60 \pm 13	62 \pm 15	0.577
Female	75 (71)	50 (68)	25 (78)	0.357
Ruptured	55 (52)	32 (44)	23 (72)	0.011
Anterior circulation	81 (77)	60 (82)	21 (66)	0.079
Aneurysmal morphology				
Maximum dome size (mm)	7.5 \pm 3.2	7.0 \pm 2.3	8.8 \pm 4.4	0.071
Neck size (mm)	4.2 \pm 1.9	3.7 \pm 1.3	5.2 \pm 2.6	0.002
Dome to neck ratio	1.9 \pm 0.9	2.0 \pm 0.6	1.8 \pm 1.3	0.022
Volume (mm ³)	244 \pm 414	159 \pm 182	438 \pm 667	0.056
Procedure technique				
Balloon neck plasty	19 (18)	10 (14)	9 (28)	0.100
Double-catheter	49 (47)	30 (41)	19 (59)	0.094
First coil				
Target 360	46 (44)	32 (44)	14(44)	0.720
Cashmere	40 (38)	28 (38)	12 (38)	
GDC-18 360	6 (6)	4 (5)	2 (6)	
Presidio-18	6 (6)	3 (4)	3 (9)	
Others	7 (7)	6 (8)	1 (3)	
PD				
Initial PD (%)	10.4 \pm 5.2	11.5 \pm 5.3	7.8 \pm 4.1	<0.001
Final PD (%)	22.7 \pm 6.3	25.4 \pm 4.1	16.3 \pm 3.8	<0.001
Recurrence	11 (11)	4 (6)	7 (22)	0.032

PD packing density, Values are n (%) or mean \pm standard deviation

Table 2 Multivariable logistic regression analysis for prediction of final PD \leq 20%

	OR	95% CI	<i>P</i> value
Initial packing density	1.22	1.03-1.45	0.025
Rupture status	0.19	0.07-0.55	0.002
Neck size	0.69	0.47-1.01	0.058
Dome to neck ratio	1.15	0.62-2.12	0.652

Table 3 Clinical characteristics of the aneurysms according to single or double catheter method

	Single catheter <i>n</i> = 56 (%)	Double catheter <i>n</i> = 49 (%)	<i>P</i> value
Ruptured	34 (61)	21 (43)	0.080
Anterior circulation	47 (84)	34 (69)	0.103
Aneurysmal morphology			
Maximum dome size (mm)	6.4 ± 1.9	8.8 ± 3.9	<0.001
Neck size (mm)	3.6 ± 1.7	4.9 ± 1.9	<0.001
Dome to neck ratio	1.9 ± 0.6	1.9 ± 1.1	0.131
Volume (mm ³)	111 ± 125	397 ± 557	<0.001
PD			
PD of first coil (%)	9.9 ± 5.0	7.1 ± 4.4	<0.001
PD of second coil (%)	-	3.9 ± 1.8	-
Initial PD (%)	9.9 ± 5.0	10.9 ± 5.5	0.185
Final PD (%)	24.2 ± 7.1	20.9 ± 4.7	0.005

PD packing density, Values are n (%) or mean ± standard deviation

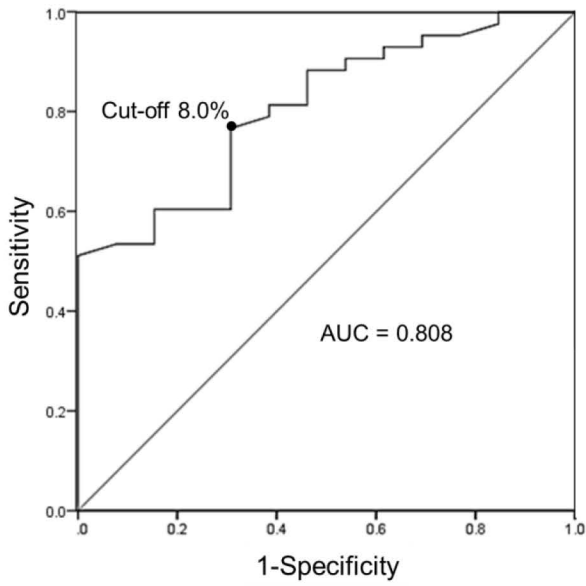
Table 4 Result of endovascular treatment according to initial PD

	Initial PD \geq cutoff values <i>n</i> = 67 (%)	Initial PD < cutoff values <i>n</i> = 38 (%)	<i>P</i> value
Final PD \geq 20%	56 (83)	17 (45)	<0.001
Initial angiographic result			
Complete occlusion	26 (39)	7 (18)	0.002
Neck remnant	29 (43)	12 (34)	
Body filling	12 (18)	19 (50)	
Recurrence	4 (6)	7 (18)	0.045

Values are *n* (%).

Figure 1

a : single catheter



b: double catheter

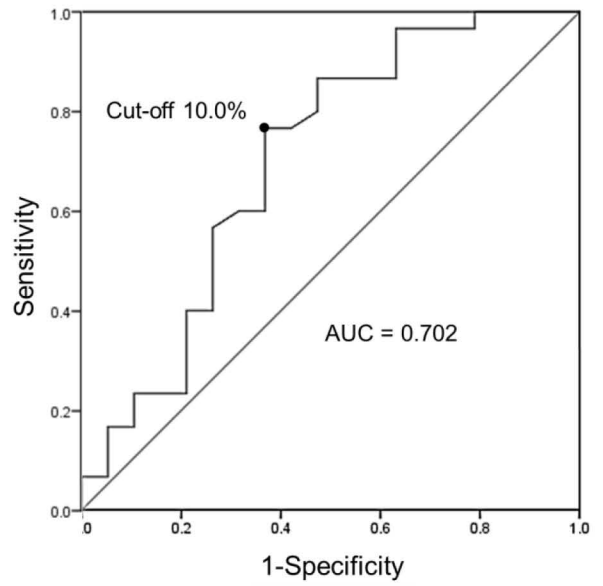


Figure 2

