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Original Article

Relationship between the Volume Rate of Ed Coil (Ed Ratio) and Packing Density in Endosaccular Embolization of Cerebral Aneurysms

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Abstract

Purpose: A high packing density (PD) (i.e., coil volume per aneurysm volume) helps prevent recanalization after endosaccular embolization of cerebral aneurysms. We hypothesized that the use of soft coils may be useful to raise PD and retrospectively investigated the correlation between the ED coil volume rate (i.e., volume ratio of all placed coils) and PD in patients treated with endosaccular embolization using this coil. **Methods:** Excluding aneurysms treated with a stent, 292 aneurysms treated using ED coils were included in this study. The 292 aneurysms and aneurysms with ≥30%, ≥40%, and ≥50% ED coil volume rates (202, 168, and 129 aneurysms, respectively) underwent linear regression analysis of the following seven factors' influence on PD:ED ratio, aneurysm volume, neck width, height, maximum diameter, dome-to-neck ratio, and aspect ratio. **Results:** Independent factors of a high PD were high ED ratio and small neck width on analyses of aneurysms with an ED ratio of ≥40% and ≥50%. Only neck width was an independent factor on analyses of all 292 aneurysms and aneurysms with ED ratio of ≥30%. **Conclusion:** The use of ED coils in high volume rate correlated with a high PD and may contribute to prevent recanalization in small aneurysms.

Keywords: *Aneurysm, ED coil, packing density, recanalization*

Introduction

Recanalization is a major problem of endosaccular embolization of cerebral aneurysms. One cause of recanalization is incomplete occlusion on embolization. One of the methods to prevent recanalization is to achieve a high packing density (PD) which is the coil volume/aneurysm volume. Piotin *et al.*[1] in an *in vitro* experiment reported that PD could be elevated using soft coils as filling coils; however, clinical evidence is lacking. ED coils are detachable coils. They are characterized by hyperflexibility of the coil region and flexibility of the tip of the pusher wire near the coil junction, which leads to low resistance during coil insertion and high catheter stability. We have performed endosaccular embolization using these coils; however, coils sold by various companies are used in combination during an actual endoaneurysmal embolization. Therefore, the ED coil volume rate (i.e., the ED ratio) varies. We investigated the relationship between ED ratio and PD to investigate its influence on tight packing. In addition, coil flexibility was evaluated by physical property testing.

Methods

ED coils (Kaneka Medix, Osaka, Japan) are platinum coils with instantaneous electric detachability, previously reported as immediately electrodetachable coil, and they are commercially available and clinically used in Japan.[2,3] The detachment mode is instantaneous through fusing polyvinyl alcohol that connects the coil and pusher wire by a 1.2 W monopolar high-frequency electric current.

ED coils can be soft or extrasoft. The former is equivalent to the Guglielmi detachable coil (GDC) 10 soft, and the latter is more flexible than the GDC ultrasoft. A reason for the hyperflexibility is the thickness of platinum stock wire of the primary coil. The thickness of extrasoft coil is 0.0014 inches, which is thinner than the thickness (0.002 inches) of the GDC ultrasoft coil. In addition, the tip of the pusher wire is flexible because of its flat cross-section structure. This reduces microcatheter instability (i.e., kick back) during coil insertion.

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Experiment on the physical property

The flexibility of the coil and tip of the pusher wire was compared between ED coil Extrasoft and GDC ultrasoft, which was the softest coil available among commercially available coils at the time of the launch of ED coils. With regard to coil flexibility, when using the ED coil Extrasoft (2 mm × 3 cm) and GDC ultrasoft (2 mm × 3 cm), one loop was free and the other regions were fixed in an acrylic block. Compression (0.01–0.25 mm) was loaded on the free loop using a microload cell (Digital Force Gauges; Shinto Scientific Co., Ltd., Tokyo, Japan) [Figure 1a]. The reaction to the pressure (mN) was measured three times. With regard to the flexibility of the pusher wire tip, the fulcrums were placed at the tip and 10 mm from the tip region as shown in Figure 1b. The lateral side of the fulcrum was fixed at 10 mm, and pressure was applied to the central region between the two fulcrums (pressed distance: 0.01–2.5 mm) using the microload cell. The reaction was measured three times.

Patients

Our institute's review board approved the data collection and statistical analyses for this study. ED coils became available in October 2006. Patients treated after this date until September 2012 (72 months) were analyzed. During this period, ED coils were used for endosaccular embolization in 345 patients. Patients with missing aneurysm volumes and ED ratio data, disposition of the coils outside the aneurysm, thrombotic aneurysm, and retreatment were excluded because the aneurysm and coil volumes could not be accurately measured. Also, those excluded were patients concomitantly treated with expandable coils (Hydrocoil; Microvention, Aliso, Viejo, California) and/or stent because these markedly influence the PD. As a result, 292 aneurysms in 289 patients were included in this analysis.

Angiography and intravascular surgery

Before treatment, diagnostic angiography was performed using 4 Fr catheters. Two-dimensional angiography and three-dimensional rotational angiography (3D-RA) were usually performed (Integris Allura; Philips Medical Systems, Best, The Netherlands). The aneurysm diameter, neck width, and volume were measured from the volume-rendered 3D images. The threshold for the volume-rendered image was fixed as the default value provided by the software. To digitally measure the aneurysm volume, the aneurysm was manually segmented from the parent artery on this 3D reconstruction image and the volume was calculated by machine software (3D-RA workstation; Philips Medical Systems, Best, The Netherlands).

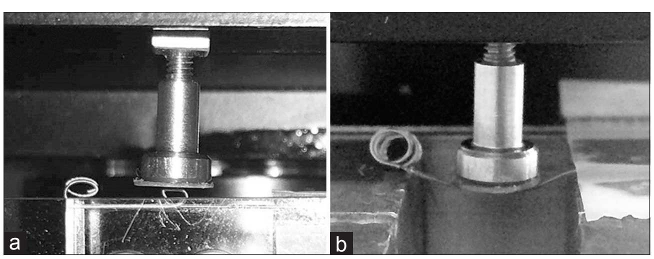

Figure 1: (a) The photograph of the measurement of coil flexibility. Except for one loop (diameter, 2 mm), the coil (ED coil Extrasoft and Guglielmi detachable coil ultrasoft) is fixed in an acrylic block and pressed stepwise by a microload cell (0.01–0.25 mm, which is measured every 0.01 mm). The reaction to the pressure (mN) is measured three times. (b) The photograph of the measurement of flexibility of the 10-mm tip of pusher wire. The pusher wire, except for the 10-mm tip, is fixed to a table. The 10-mm tip is floated in the air without support, and the pressure is loaded to this region using the microload cell (0.01–1.5 mm, which is measured every 0.01 mm). The reactions of ED coil Extrasoft and Guglielmi detachable coil ultrasoft are measured three times. GDC: Guglielmi detachable coil

A transfemoral approach was used in most patients. A balloon-assisted technique was primarily employed for endosaccular embolization. A balloon catheter was nearly always prepared and positioned at the neck because it is effective for neck remodeling and flow control when an intraoperative rupture occurs. It was inflated if necessary. For irregularly shaped aneurysms with multiple domes or for very large aneurysms, a double catheter technique was occasionally employed in conjunction with the balloon remodeling technique. In this method, coil placement could be homogenous in the aneurysm sac. Since September 2011, stents for aneurysm treatment have been available and are used in some highly selected cases such as fusiform aneurysms and wide-necked aneurysms for which the balloon remodeling technique is ineffective. These stent-assisted cases were excluded from this analysis.

With regard to coil selection, 18-type coils with a large primary diameter (as many as possible) were used in the early phase (i.e., framing and the early half of filling) for large aneurysms with a diameter of 10 mm or larger (0.0135–0.015 inches; GDC 18 or 18 soft; Stryker, Kalamazoo, MI, USA or Microplex Cosmos 18, Microvention, Los Angeles, CA, USA), followed by some of ED coils, GDC 10, Trufill DCS and Orbit Galaxy (Johnson and Johnson Codman, Miami, FL, USA), and Axium (EV3 Endovascular Inc., Plymouth, MN, USA) with a smaller primary diameter. For small aneurysms with a diameter smaller than 10 mm, several 18-type coils or 10-type coils with a 3D shape were used in the early phase, followed by softer coils (ED coil, GDC 10, Axium). With regard to the differential use of ED coil Soft and ED coil Extrasoft, the former coil was used for a diameter of 5 mm or greater and the latter coil was used for a diameter of 4 mm or smaller because the variations of the secondary coil diameter ranged 2–10 mm and 1.5–5 mm, respectively.

These rough selection criteria were common to the operators, but coils sold by various companies were used in combination with regard to the conditions in the actual practice of endosaccular embolization. The coil volume was calculated using the equation, $V = \pi\ (P/2)^2L$, in which "L" represents the coil length and "P" represents the primary coil diameter. The PD was calculated by coil volume/aneurysm volume × 100%. A PD of 20% was set as the minimum requirement for embolization and PD was calculated every time a coil was inserted.

Data collection

The following data for aneurysms were collected from medical records and complemented by repeat measurements from the 3D-RA images: PD, rupture status at presentation (i.e., ruptured or unruptured), aneurysm location (i.e., anterior or posterior circulation), aneurysm volume (V), neck width (N), and three diameters (i.e., height [H], width [D1], and the width perpendicular to D1 [D2]) as shown in Figure 2. The largest value among H, D1, and D2 was defined as the maximum diameter for each aneurysm. The dome-to-neck ratio (DNR) was calculated as the ratio of the mean of D1 and D2 to N ([D1 + D2]/2N]). The aspect ratio (AR) was calculated as the ratio of the height to neck width.

Recanalization and its risk factor

Follow-up imaging with DSA or MRA of more than 6 months after the endovascular surgery was performed for 241 aneurysms. A recanalization was defined as any increased flow in the aneurysmal sac. The recanalization was qualified as major if its recanalized space was saccular shape and large enough for the insertion of coils. Frequency of recanalization was investigated, and risk factors for the major recanalization were statistically analyzed.

Statistical analysis

For all 292 aneurysms and those with an ED ratio of ≥30%, ≥40%, and ≥50% (202, 168, and 129 aneurysms, respectively), the influence of the following seven factors on the PD was investigated using linear regression analysis: ED ratio (i.e., volume ratio) and six morphological variables (aneurysm volume, neck width, height, maximum diameter, DNR, and AR). Items for which a significant ($P < 0.05$) regression equation was obtained on single regression analysis were subjected to multivariate analysis using multiple regression analysis.

With regard to the risk factors for recanalization, influence of rupture status, neck width, residual aneurysm volume at the time of procedure (RV) was investigated using multivariate logistic regression analysis. The RV was calculated by the following equation, RV = aneurysm volume × (1 − PD/100).

The Excel Toukei 2012 statistical analysis software (Social Survey Research Information Co. Ltd., Tokyo, Japan) was used.

Results

The three measured values of coil loop reaction to pressure are presented by the graph [Figure 3a]. For example, the reactions of ED coil and GDC to 0.1-mm pressure were 1.1 ± 0.1 mN (mean ± standard deviation [SD]) and 2.0 ± 0.2 mN, respectively, and their reactions to a 0.2-mm pressure were 2.2 ± 0.5 mN and 4.7 ± 0.4 mN, respectively. This indicates that the reaction of the ED coil was approximately one-half that of the GDC ultrasoft. The reactions of the pusher wire tip to pressure are similarly presented by a graph [Figure 3b]. The reactions of ED coil pusher and GDC pusher to 0.5-mm pressure were 13.4 ± 0.2 mN and 21.1 ± 0.4 mN, respectively, and their reactions to the 1.5-mm pressure were 31.8 ± 0.4 mN and 65.2 ± 0.6 mN,

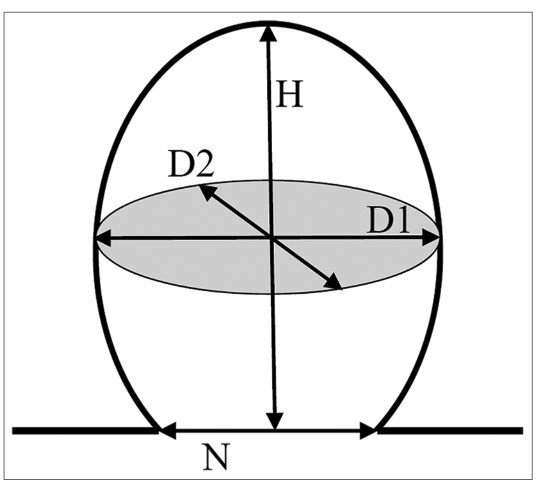

Figure 2: Scheme of the measurement of the morphological parameters of an aneurysm. The aspect ratio is calculated as height/neck. The dome-to-neck ratio is calculated as (D1 + D2)/2N. H: Height, N: Neck, D1: Width (D1), D2: Width vertical to D1

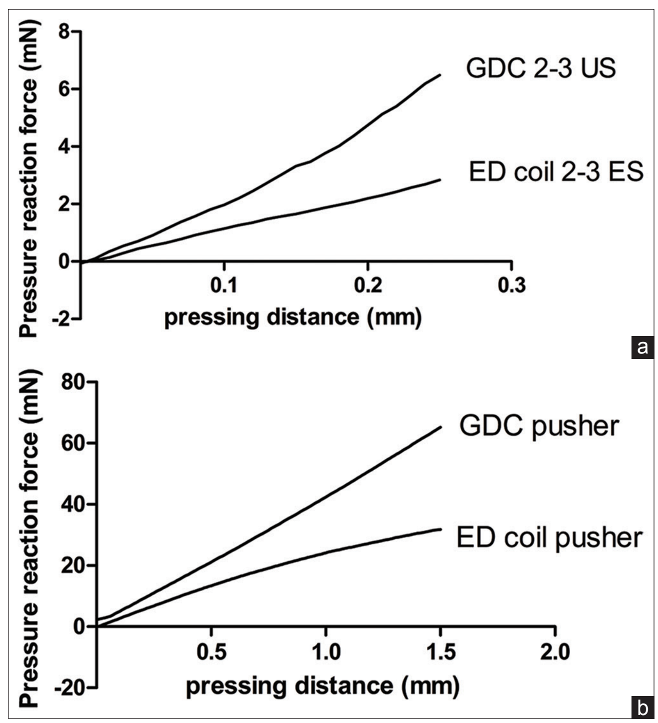

Figure 3: (a) The results of the physical property experiment of the reaction of the coil loop to pressure. One loop each of the ED coil Extrasoft (2 mm × 3 cm) and Guglielmi detachable coil ultrasoft (2 mm × 3 cm) coils is pressed using the microload cell. The pressed distance and reaction are measured three times and plotted. (b) The reaction of the pusher wire tip to pressure. The pressed distances and reactions of the pusher wire tip of ED coil Extrasoft (2 mm × 3 cm) and Guglielmi detachable coil ultrasoft (2 mm × 3 cm) are measured three times and plotted

respectively, which indicates that the reaction of ED coil pusher was also approximately one-half that of the GDC.

Baseline characteristics of clinical cases

Two hundred sixty-one aneurysms were small (maximum diameter, <10 mm), 31 aneurysms were large (diameter, 10–25 mm), and 0 aneurysms were giant (diameter, ≥25 mm). Fifty-six aneurysms were in posterior circulation and 236 aneurysms were in anterior circulation. Fifty-three aneurysms were ruptured and 239 aneurysms were unruptured. The ED ratio (volume ratio in all placed coils) of the 292 aneurysms was 46.5% ±25.4% (mean ± SD; range, 1.1%–100%). The PD of the 292 aneurysms was 21.3% ± 5.5% (mean ± SD; range, 5.4%–41.1%). A PD of 20% or higher was achieved in 179 (61.3%) aneurysms. Angiographic results of endosaccular embolization were complete occlusion in 156 aneurysms (53.4%), neck remnant in 91 (31.2%), and body filling in 45 (15.4%). Recanalization occurred in 29 (12.0%) in the followed up 241 aneurysms. Among these, major recanalization was in 15 (6.2%) and 11 aneurysms (4.6%) underwent retreatment.

Correlation between the ED ratio and the Packing Density

The correlation between each factor and PD was analyzed for all 292 aneurysms using single regression analysis. Significant correlations were detected in the ED ratio, AR, DNR, neck width, max size, and volume. When these factors were subjected to multiple regression analysis, only neck width showed a significant correlation. The ED coil volume rate had a marginally significant correlation with PD (P = 0.089). Similar findings were noted in 202 aneurysms with an ED ratio of 30% or higher. For 168 aneurysms with an ED ratio of 40% or higher, single regression analysis showed that ED ratio, AR, neck width, and volume were significant factors, and multiple regression analysis showed that neck width (P = 0.025) and ED ratio (P = 0.006) were significant factors. For 129 aneurysms with an ED ratio of 50% or higher, the neck width (P = 0.032) and ED ratio (P = 0.008) were similarly significant factors on multiple regression analysis [Table 1 and Figure 4]. Although the R^2 values in the correlation between ED ratio and PD is not high, that for aneurysms with ED ratio ≥50% is similar value with R^2 in the correlation of the neck width and PD.

With regard to the risk factors for major recanalization, multivariate logistic regression analysis showed that ruptured aneurysm (P = 0.002; OR = 0.109; 95%CI = 0.028–0.432) and large residual volume (P = 0.001, OR = 0.011; 95% CI = 0.001–0.178) were the independent risk factors but not neck width [Table 2].

Table 1: Univariate (upper) and multivariate (lower) linear regression analysis of the factors influencing the packing density

Variables	All aneurysms (n=292)			ED ratio 30% (n=202)			ED ratio 40% (n=168)			ED ratio 50% (n=129)		
	P	Standardized β coefficient	SE	P	Standardized β coefficient	SE	P	Standardized β coefficient	SE	P	Standardized β coefficient	SE
Univariate linear regression analysis												
ED ratio	**0.013**	0.146	0.013	**0.004**	0.204	0.02	**0.0003**	0.274	0.023	**0.0008**	0.292	0.028
Aspect ratio	**0.0004**	0.206	0.408	**0.007**	0.188	0.472	**0.021**	0.177	0.489	**0.033**	0.188	0.555
Dome/neck ratio	**0.016**	0.141	0.547	**0.032**	0.151	0.658	0.104	0.126	0.666	0.16	0.124	0.743
Neck width	**<0.0001**	−0.300	0.187	**<0.0001**	−0.343	0.264	**<0.0001**	−0.325	0.301	**0.0009**	−0.289	0.347
Maximum diameter	**0.014**	−0.144	0.123	**0.055**	−0.135	0.171	0.079	−0.136	0.175	0.44	−0.069	0.199
Height	0.732	−0.020	0.156	0.465	−0.052	0.207	0.453	−0.058	0.216	0.979	0.002	0.244
Aneurysm volume	**0.036**	−0.123	1.267	**0.017**	−0.167	2.318	**0.023**	−0.175	2.359	0.37	−0.08	2.945
Multivariate linear regression analysis												
ED ratio	0.089	0.099	0.013	0.065	0.130	0.020	**0.006**	0.207	0.023	**0.008**	0.233	0.028
Aspect ratio	0.483	0.07	0.708	0.698	−0.046	0.810	0.966	−0.004	0.634	0.709	0.036	0.619
Dome/neck ratio	0.63	−0.045	0.870	0.802	0.028	1.046						
Neck width	**0.006**	−0.319	0.386	**0.002**	−0.369	0.478	**0.025**	−0.295	0.533	**0.032**	−0.214	0.403
Maximum diameter	0.733	0.047	0.291									
Aneurysm volume	0.694	0.042	2.330	0.493	0.071	3.415	0.815	0.026	3.432			

P<0.05 were shown in bold. ED ratio – Volume ratio of implanted ED coil to total coils; SE – Standard error

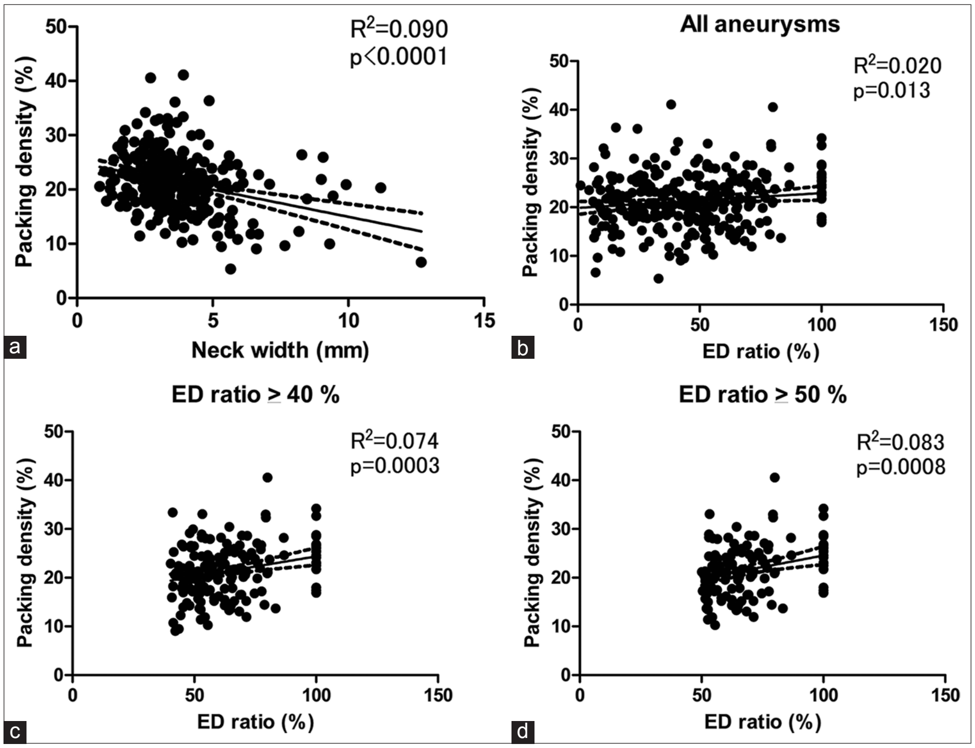

Figure 4: (a) Linear regression analysis between neck width and packing density, (b) linear regression analysis between ED ratio and packing density in all 292 aneurysms, (c) linear regression analysis between ED ratio and packing density in aneurysms with ED ratio ≥40% (*n* = 168), (d) linear regression analysis between ED ratio and packing density in aneurysms with ED ratio ≥50% (*n* = 129). Both ED ratio and neck width had significant correlation with packing density. With higher ED ratio, R^2 became higher and close to that of neck width

Table 2: Multivariate logistic regression analysis of factor influencing recanalization on follow-up study

Variables	*P*	OR	95% CI	
			Lower	Upper
Ruptured aneurysm	**0.002**	0.109	0.028	0.432
Neck width	0.861	0.967	0.664	1.407
Volume of residual aneurysm lumen	**0.001**	0.011	0.001	0.178

P<0.05 were shown in bold; OR – Odds ratio; CI – Confidence interval

Discussion

Recanalization is one of drawbacks of endoaneurysmal embolization of cerebral aneurysms. One cause is incomplete occlusion on embolization.[4-6] It has previously been reported that PD of 20%–25% or higher is useful for preventing recanalization; therefore, achieving a PD of at least 20% is an important target of endoaneurysmal embolization.[7-12] In the present study, though the PD itself was not an independent risk factor for recanalization (data not shown), absolute volume of residual aneurysm lumen calculated from aneurysm volume and PD was an independent risk factor. Therefore, the larger the aneurysm volume, the higher PD has to be achieved to prevent recanalization.

In an experimental study on the influence of flexible coils on PD, Piotin *et al*.[1] reported that flexible coils were useful in increasing the PD in their experiment in which they used a silicone aneurysm model.

Based on the results of the physical property experiment, the reactions of the coil loop and the delivery wire tip of the ED coil Extrasoft were approximately one-half of the reaction of the GDC ultrasoft, which indicates that the ED coil is very soft. The softness of the coils allows the coils to fit readily into small irregular spaces and the softness of the pusher wire reduces straightening of the microcatheter as the top closely approaches the microcatheter tip. These factors reduce the risk that the microcatheter is pushed out (i.e., on the parent artery side) by the reaction to coil insertion in the early phase. Many coils can be placed as long as the catheter is retained in the aneurysm, which contributes to dense packing. This is the same for the pusher wire of the ED coil Soft.

It has been reported that the diameter of the stock wire markedly contributes to coil flexibility.[13,14] The stock wire diameter of ED coil Extrasoft is smaller than the diameter of GDC ultrasoft. On analysis of clinical cases, a low ED ratio did not significantly contribute to the elevation of the PD, but it did significantly contribute to the elevation of the PD when the volume ratio was 40% or higher. In aneurysms with a low ED ratio, the ED coils were used only for finishing step of coiling. In aneurysms with a high ED ratio, the use of ED coils was initiated in filling, which is an early step. Their use in an early step may have reduced the kick back of microcatheters. Many coils can be delivered because the microcatheter remains in the aneurysm for a prolonged time, thereby contributing to the elevation of the PD.

Based on previous reports, our institution targets a PD of 20% or higher by simultaneously calculating the PD with coiling. This has clarified that the use of ED coils is also useful to achieve this target. A small neck width was also an independent factor of high PD. This is not contradictory because several studies have reported that a wide-necked aneurysm is a factor that makes endoaneurysmal embolization difficult.[15-18] This finding is widely recognized.

Factors influencing the PD may include coil thickness and the shape of the secondary coils as well. There have been several reports stating that the Penumbra coil 400 (Penumbra Inc. San Leandro, CA, USA) is useful for increasing the PD because the diameter of its primary coil is the largest among coils available.[19,20] However, the diameter of compatible microcatheters is also large. Thus, we use it for large or giant aneurysms. In this study, the aneurysms were small in most patients; therefore, the Penumbra coil was not used in any patient. So-called "18-type" coils (primary coil diameter, 0.0135–0.015 in) are also useful for increasing the PD and these are frequently used for large or giant aneurysms. A few coils are used for small aneurysms of 7–8 mm or larger but not for aneurysms smaller than this. Thus, the maximum diameter and ratio of 18-type coils should be linked; however, no correlation existed between the maximum diameter and the PD. When using 18-type coils, the microcatheter tip is frequently kicked out of the aneurysm even in the early stage of coiling and that may disturb dense packing.

Coils with a spherical shape or a 3D shape more markedly contribute to elevation of the PD, compared to helical coils.[21-23] The reasons for this finding is that coils with these shapes readily fit into the aneurysm, even if the neck is broad, and a homogenous basket is readily formed within aneurysms. Because ED coils are very flexible, even though they are two-dimensional helical coils, the loops easily fold and form a 3D shape that corresponds to the shape of the residual lumen, which may contribute to elevation of PD. However, in most patients, other coils with a 3D shape were used in the initial step because the coils are likely to deviate from the neck of broad-necked aneurysms during the formation of the initial basket.

In previous reports on the clinical use of ED coils, Harada and Morioka[24] used ED coils in the final step in 92 aneurysms. They investigated the correlations between the ED ratio, DNR, maximum size, aneurysm volume, and PD. They observed that the ED ratio and maximum aneurysm diameter were correlated with PD. Our analysis was different from their study with regard to the following points: The number of patients was large; the ED coil Extrasoft and ED coil Soft were included in analysis; the ED coils were actively used from the filling step, rather than only in the final step; and the mean ED ratio was 46.5% ± 25.4%, which was slightly higher than the ED ratio (40.5% ± 25.1%) in their study.

The limitations of this analysis were that the conclusion cannot be applied to large or giant aneurysms because the aneurysms treated with ED coils were mostly small. Furthermore, this study was a retrospective analysis and the PD may have been influenced by other geometrical features such as the axial angles of the parent artery and aneurysms and the presence of blebs, in particular, blebs close to the neck that are difficult to occlude. With regard to the embolization method, patients concomitantly treated with a stent or hydrocoils were excluded; however, other adjunctive techniques such as the double catheter technique were applied in a small number of patients. The influences of these factors were not considered.

Conclusion

The use of ED coils in high volume rate correlated with a high PD in small aneurysms. In other words, in general, very flexible coil with soft pusher wire is useful to raise PD and may contribute to prevent recanalization.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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