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ORIGINAL ARTICLE

Effects of anatomic characteristics of aneurysms on packing density in endovascular coil embolization: analysis of a single center's experience

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Abstract When embolizing cerebral aneurysms, dense coil packing may prevent recanalization but this may be influenced by the aneurysm morphology. We have analyzed retrospectively the relationship between anatomic features and the volumetric coil packing density. We analyzed 452 aneurysms in 434 patients treated by coil embolization without stenting, expressing packing density as volume embolization ratio (VER, volume of inserted coils/aneurysm volume). Six morphological variables (neck width, height, maximum diameter, dome to neck ratio (DNR), and aspect ratio), aneurysm location, and whether the aneurysm was ruptured or unruptured were analyzed with respect to dense (VER ≥20 %) or loose (VER <20 %) packing densities, using logistic regression analysis and ROC analysis. Among 452 aneurysms, VERs >20 % were achieved for 272 aneurysms, with a mean VER of 24.7 %. The mean VER of the remaining 180 aneurysms was 15.6 %. In univariate analyses, the predictors for dense packing were having an anterior circulation, DNR, aspect ratio, and neck width. In multivariate analysis, the independent predictors were smaller neck width (odds ratio (OR) 0.8735; 95 % confidence interval (CI) 0.7635–0.9993) and larger aspect ratio (OR 1.6679; 95 % CI 1.0460–2.6594). ROC analysis showed optimal cutoff values for an aspect ratio of 1.35 (sensitivity 69.5 %, specificity 51.7 %) and a neck width of 3.13 mm (sensitivity 51.1 %, specificity 27.8 %). Although dense coil packing is still difficult to achieve in wide-necked aneurysms without the use of stents, packing with VER >20 % is expected to be achieved when the height is 1.35 times larger than the neck width.

Keywords Aneurysm · Morphology · Aspect ratio · Packing density · Coiling

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Introduction

Recanalization is a major problem in the embolization of cerebral aneurysms. It is well known that packing coils as tightly as possible is important to avoid recanalization and that incomplete embolization is one of the major risk factors for recanalization [4, 18, 23]. To evaluate the tightness of coil embolization, the volume embolization ratio (VER: coil volume/aneurysm volume × 100 %) is a useful index, with VERs greater than 20–25 % reported to be effective in avoiding recanalization [13, 14, 26–29].

The morphological features of aneurysms vary and are well known to affect their amenability to endosaccular coil embolization. Since the 1990s, wide-necked aneurysms have been said to be difficult to embolize as a coil easily herniates from the neck. The neck width and dome to neck ratio (DNR) have been identified as predictive factors for incomplete embolization [6, 7, 11, 15]. An aneurysm with a low aspect ratio (<1.2) has also recently been said to be difficult to embolize without using an adjunctive technique such as balloon remodeling or a stent-assisted technique [2]. However, the relationship of VER and various morphological features has not yet been adequately investigated. We have therefore reviewed the morphological features of aneurysms treated at our institute and retrospectively analyzed their relationship to VER.

Materials and methods

Patients

Our institute's review board approved the data collection and statistical analyses for this study. The medical records and angiograms for 508 consecutive patients suffering 551 aneurysms, who had been treated by endovascular surgery at our institute between 2006 and 2012, were reviewed.

The following cases for which VER data and/or aneurysm volume were unavailable were excluded from the analysis: cases of retreatment, parent artery occlusions, partially thrombosed aneurysms, presence of extrasaccular coils due to procedural rupture or protrusion to the parent artery and embolization with expandable coils (Hydrocoil; Microvention, Aliso, Viejo, California). Cases of stent-assisted embolization were also excluded because the stent assistance greatly influences the packing density in wide-necked aneurysms. After these exclusions, 452 aneurysms in 434 patients were included in the statistical analysis.

Angiography and endovascular surgery

Prior to treatment, diagnostic angiography was carried out using 4F catheters. Usually, two-dimensional angiography and three-dimensional rotational angiography (3D-RA) were used (Integris Allura; Philips Medical Systems, Best, the Netherlands). The aneurysm diameter, neck width, and volume were measured from volume-rendered 3D images using a default value as a threshold. The detailed methodology for 3D-RA and the measurement of aneurysm volume is as follows. Fifteen milliliters of nonionic contrast medium was injected through a 4F catheter by use of an injector with a velocity of 3 mL/s. Image acquisition started 1 s after the start of the injection. The acquisition time of images was 4 s. Volume-rendered 3D images were reconstructed with a 100 % magnification and a matrix of 256×256×256 pixel by using the machine software. 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 and volume was calculated by using machine software (3D-RA workstation, Philips Medical Systems, Best, the Netherlands).

In most cases, the procedure used a transfemoral approach. A balloon-assisted technique was primarily employed for endosaccular embolization. A balloon catheter was almost always prepared and positioned at the neck, as it is effective for neck remodeling and flow control when intraoperative rupture occurs, and inflated if necessary. Therefore, in case of a very small neck aneurysm, a balloon is primarily prepared for intraoperative rupture and is not often actually inflated.

A double catheter technique was occasionally employed, in conjunction with the balloon remodeling technique, for irregularly shaped aneurysms with multiple domes or for very large or giant aneurysms, so that coil placement could be continued in cases where premature withdrawal of one microcatheter occurred. Since September 2011, stent for aneurysm treatment has been available and was used in some highly selected cases, such as fusiform aneurysms and wide-necked aneurysms, for which a balloon remodeling technique is still ineffective. These stent-assisted cases were also excluded from this analysis.

The working angle was set and the coiling procedure was started using 3D-shaped coils in almost all cases. A balloon catheter was inflated if remodeling was needed. For middle-sized aneurysms (diameter >7–8 mm), thicker coils (diameter=0.0135–0.015 in.) were used from the start. Softer coils of either helical or 3D shape were used as filling and finishing coils.

The coil volume was calculated using the equation: $V=\pi(p/2)^2L$, where L represents the coil length, and p represents the primary coil diameter. VER was calculated as coil volume/aneurysm volume×100 %. A VER of 20 % was set as the minimum requirement for embolization and VER was calculated every time a coil was inserted. This VER value of minimum requirement is derived from previous investigations by several authors. Optimal VERs to prevent recanalization were reported to be greater than 20–25 % when the aneurysm volume is approximately calculated from 2D angiogram [13, 14, 27–29]. And the value was revised to 15.5–19.4 % based on a work clarifying that the aneurysm volume measured using 3D-RA is 1.26–1.29 times larger than the approximation from 2D angiogram [25]. Therefore, 20 % was set as minimum requirement in our practice.

Data collection and statistical analysis

The following data for aneurysms were collected from medical records and complemented by repeat measurements from 3D-RA images: VER, rupture status at presentation (ruptured or unruptured), aneurysm location (anterior or posterior circulation), aneurysm volume (V), neck width (N), and three diameters, height (H), width ($D1$), and another width perpendicular to $D1$($D2$), as shown in Fig. 1. The largest value among H, $D1$, and $D2$ was defined as the maximum diameter (max$D$) 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 (H/N). The VERs were categorized as densely packed (VER ≥20 %) and loosely packed (VER <20 %).

Univariate logistic regression analysis was carried out for VER (densely or loosely packed) and eight variables, as described above: max$D$, H, N, AR, DNR, V, ruptured or not, and anterior or posterior circulation. For variables found to be

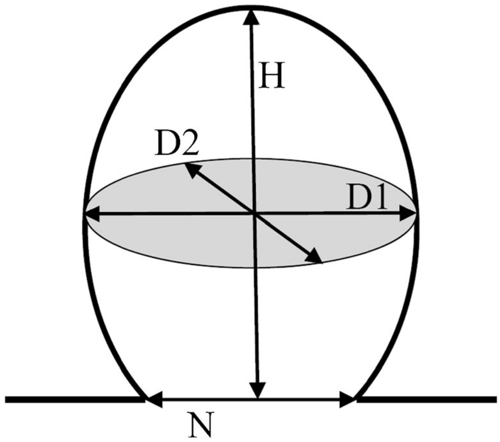

Fig. 1 Diagram showing measurements made of the morphological parameters of an aneurysm. *H* height, *N* neck, *D1* width, *D2* width perpendicular to D1. Aspect ratio is calculated as *H/N*. Dome to neck ratio is calculated as $D1+D2/2N$

significant by univariate analysis, a multivariable logistic regression analysis was carried out to determine independent predictors of dense packing (VER ≥20 %). The predictive accuracy of the independent predictors for dense packing was assessed by calculating the area under the receiver operating characteristic (ROC) curves. Optimal cutoff values were chosen as the point on the ROC curve closest to the top left corner. Statistical analyses used Excel Toukei 2012 software (Social Survey Research Information Co. Ltd., Tokyo Japan.)

Results

Among the 434 patients, 107 were male and 327 were female and their mean age was 60.1 years. Among the 452 aneurysms, a VER ≥20 % was achieved for 272 aneurysms, with a mean VER of 24.7 %. The mean VER of the remaining 180 aneurysms was 15.6 %. The baseline categories and characteristics for the 452 aneurysms in 434 patients are shown in Tables 1 and 2.

Univariate logistic regression analysis showed that anterior circulation, larger dome to neck ratios, larger aspect ratios, and smaller neck width values were significantly related to dense packing (p=0.0072, 0.0002, <0.0001, <0.0001, respectively; see Table 3). Multivariate logistic regression analysis showed that larger aspect ratios (odds ratio (OR) 1.6679; 95 % confidence interval (CI) 1.0460–2.6594) and smaller neck width values (OR 0.8735; 95 % CI 0.7635–0.9993) were independent predictive variables (Table 4).

ROC analysis showed that the optimal cutoff value of the aspect ratio for predicting dense packing was 1.35 (area under curve=0.6305) with a sensitivity of 69.5 % and specificity of 51.7 %. The optimal cutoff value for neck width was 3.13 mm (area under curve=0.6259) with a sensitivity of 51.1 % and specificity of 27.8 %.

Table 1 Baseline categorization of 452 aneurysms in 434 patients

Category	No. of aneurysms	No. of aneurysms with VER ≥20 % (total=272)	No. of aneurysms with VER <20 % (total=180)
Ruptured	95	55	40
Unruptured	357	217	140
Anterior circulation	360	228	132
Posterior circulation	92	44	48

Discussion

Since the Guglielmi detachable coil (GDC) was developed in the early 1990s [9, 10], endovascular surgery for cerebral aneurysms has made great advances. However, the constantly present risk of recanalization is a major drawback of coil embolization compared with clipping surgery. Recanalization sometimes leads to rebleeding in ruptured aneurysm [12] and, although it rarely leads to bleeding in unruptured aneurysm, it needs continuous, long-term, follow-up radiological examinations [8, 19]. The causes of recanalization are multifactorial and loose coil packing is one of the major factors [4, 18, 23].

Several authors have investigated the relationship between coil packing density (VER) and recanalization and have suggested that VERs greater than 20–25 % are likely to prevent coil compaction [13, 14, 26–29]. In most of these reports, with the exception of Sluzewski, et al., aneurysm volume was

Table 2 Baseline characteristics of 452 aneurysms in 434 patients

Characteristic	Mean±SD	Mean±SD	Mean±SD
	For 452 aneurysms	For aneurysms with VER ≥20 % (total=272)	For aneurysms with VER <20 % (total=180)
Aspect ratio	1.66±0.73	1.79±0.81	1.46±0.53
Dome to neck ratio	1.55±0.55	1.63±0.61	1.43±0.41
Neck width (mm)	3.74±1.70	3.46±1.51	4.17±1.88
Maximum diameter (mm)	6.64±3.02	6.45±2.93	6.93±3.13
Height (mm)	5.67±2.59	5.68±2.56	5.64±2.65
Aneurysm volume (cm^3)	0.18±0.33	0.16±0.28	0.20±0.38
VER (%)	21.11±6.17	24.71±4.78	15.64±3.39

VER volume embolization ratio

Table 3 Univariate logistic regression analysis of predictors of success of dense coil packing in aneurysms

Variable	*P* value	OR	98 % CI of OR
Ruptured or unruptured	0.6092	1.1273	0.7121–1.7846
Anterior or posterior circulation	0.0072	1.8843	1.1874–2.9903
Aspect ratio	<0.0001	2.2455	1.5852–3.1808
Dome to neck ratio	0.0002	2.424	1.5135–3.8823
Neck width	<0.0001	0.7772	0.6893–0.8764
Maximum diameter	0.1008	0.9491	0.8917–1.0102
Height	0.8672	1.0063	0.9353–1.0826
Aneurysm volume	0.2451	0.7082	0.3958–1.2671

estimated from 3 diameters (*A*, *B*, and *C*) measured in 2-dimensional angiograms, using the formula: $V=4/3\ \pi\ (A/2)\ (B/2)\ (C/2)$. It has previously been reported that volume calculations using the software supplied with the 3D-RA workstation (Philips Medical Systems) is on average 1.26–1.29 times larger than the approximate volumes obtained using the conventional formula [25]. Therefore, the conventionally recommended VER of 20–25 % can be roughly interpreted as 15.5–19.4 % when the volume is digitally measured using 3D-RA, and a VER of 20 % was set as the minimum requirement in our practice. It may be controversial to set a single VER value as a goal, because in vitro experiments and computational fluid dynamic studies have shown that a hemodynamically effective VER is dependent on neck size, lateral wall type or terminal type, and the angle made by a sac and its parent artery [1, 20]. Therefore, 20 % of VER is always a minimum requirement and we aim to embolize as densely as possible.

To achieve a VER of 20 % or more, aneurysm morphology, coil selection, and the selection of an adjunctive technique may be important factors. As to aneurysm morphology, wide-necked aneurysms have been said to be difficult to embolize [6, 7, 11, 15]. Neck widths over 4 mm and dome to neck ratios over 2.0 have been used to define aneurysms likely to be difficult to embolize [6, 7]. To treat such aneurysms, the balloon remodeling technique was first developed [5, 17], then 3D-shaped coils were introduced [3, 21], and recently, the stent-assisted technique has become available. With the use of a stent, very wide-necked aneurysms and even fusiform aneurysms can now be treated. However, intensive and prolonged use of antiplatelet medication is required [24], which limits the use of stents for ruptured aneurysms and for patients who cannot tolerate long-term antiplatelet medication, such as patients with cancer who may need major surgery and young women who want to become pregnant in the future. Therefore, coil embolization without stenting is still the first choice for endosaccular embolization and it is important to be able to predict if an aneurysm is likely to be successfully embolized with coils alone, with or without using the balloon remodeling technique, or whether stenting is inevitable.

Table 4 Multivariate logistic regression analysis of predictors of success of dense coil packing in aneurysms

Variables	*P* value	OR	98 % CI of OR
Neck width	*0.0489*	0.8735	0.7635–0.9993
Dome to neck ratio	0.4297	1.277	0.6961–2.3427
Aspect ratio	*0.0316*	1.6679	1.046–2.6594
Anterior or posterior circulation	0.0599	1.5988	0.9807–2.6065

$P<0.05$ is defined as statistically significant

Wide-necked aneurysms are still difficult to embolize, but our results suggest that when the height of the aneurysm above the neck (*H* in Fig. 1) is large, countermeasures such as using 3D-shaped coils and the balloon remodeling technique enables successful coil embolization without stenting. Once the first coil basket has been successfully made, the use of the recently introduced filling coils of variable shape and softness should also improve the probability of achieving a higher VER. Brinjikji et al. previously reported that the aspect ratio was an independent predictor of the need to use adjunctive techniques such as balloon remodeling and stenting, as they employed simple coiling without balloon or stenting as their methodology of first choice; neck width and dome to neck ratio were identified as significant factors in univariate analyses but not in multivariate analysis [2]. Although our treatment strategy is somewhat different, in using balloon remodeling as a baseline technique in our procedure and using a different endpoint for our study, our results are coherent with these results. Both aspect ratio and neck width were independent predictors for dense packing in our analysis, although from ROC analysis, the aspect ratio was a more reliable predictor, with a higher sensitivity and specificity than neck width. Although VER alone does not determine the risk of recanalization, this study may contribute to how we can use data from angiograms to predict whether dense packing can be achieved with balloon remodeling, or whether stenting is needed.

The limitations of this study are its retrospective design and the limited number of factors that have been analyzed. Some other morphological features that may influence VER, but were not include in this study, include the presence of blebs, an irregular shape, and lateral wall versus bifurcation aneurysms. The selection of coil, in terms of shape, primary diameter, and softness, may also influence VER [16, 22], but were not controlled in this study and were based on the subjective decisions of individual operators, although this tends not to differ greatly within a single institute.

Balloon neck remodeling technique was used in most cases in this study, although data of whether a balloon was actually inflated or not in every case are absent. As balloon neck remodeling may raise VER, this study results can not be applied when the balloon-assisted technique is not feasible. Immediate and follow-up angiographic results are also absent. Especially the follow-up results are important to validate VER of 20 % as the minimum requirement to prevent recanalization, though the value is derived from previous several studies with follow-up data. Such follow-up data may enable a sensitivity analysis of candidates of packing densities to determine the optimal VER to achieve long-term occlusion.

Conclusions

Higher aspect ratios and smaller neck widths are independent predictors for densely packed aneurysms with VERs of 20 % or more in endosaccular coil embolization without the use of stents. Although dense coil packing is still difficult for a wide-necked aneurysm without using a stent, packing with VER >20 % is expected to be achieved when the height is 1.35 times larger than the neck width.

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Comments

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The authors investigated the degree of coil packing density as a function of aneurysm anatomy in aneurysms treated without stent assistance. This single-center experience included 434 patients with 452 aneurysms and determined the factors that influence whether an aneurysm was considered "densely packed" (≥20 %) or "loosely packed" (<20 %), as calculated by three-dimensional rotational angiographic (3D-RA) reconstructions and coil dimensions. The authors sought to define anatomical variables that could predict whether an aneurysm was likely to be densely or loosely packed using area under the curve analyses, with the hypothesis that densely packed aneurysms are less likely to recur. They found that an aneurysm aspect ratio of ≥1.35 was associated with dense coil packing. The manuscript's strengths include a large number of aneurysms and the use of 3DRA to calculate aneurysm volume (rather than conventional 2D measurements).

Many studies have attempted to relate aneurysm morphological characteristics to clinical events such as rupture risk, though the variability and imprecision of published results reduces confidence in the clinical applicability of such measures. However, the utility of this paper's conclusions (the predictor of whether dense packing is more likely) can be directly applied to clinical practice. Specifically, by determining whether a particular aneurysm is likely to be densely packed based on pretreatment morphology, a clinician could judge whether stent assistance (and its accompanying requirement for antiplatelet medications) might be required or avoided. Further prospective study is necessary, however, to validate the predictive value of this analysis, as well as the threshold of 20 % packing density (as determined by 3DRA), as they relate to aneurysm recanalization.

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This is a well-written retrospective single-center review of the assessment of the aneurysm morphology to determine the packing density achievable without the use of stent. Packing density is considered an important aspect of coiling that determines recanalization among other factors. The dome to neck ratio along with aspect ratios as performed in this article can be used as guidance for analyzing an angiogram before coil embolization to determine the need for premedication with anti-platelets and prepare for a stent assistance to achieve a minimum of 20 % packing density. Though similar packing density and remodeling can be achieved with balloon assistance compared to use of stent in most aneurysms, there is a risk of coil prolapse following balloon deflation. Today, with advanced technology, even in patients with lower aspect ratio (<1.35) the strategy may involve balloon remodeling and dense packing of aneurysm followed by placement of stent through the balloon catheter to stabilize the densely packed coil mass if needed.