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# Packing Density Necessary to Reach a High Complete Occlusion Rate in Circumferential Unruptured Intracranial Aneurysms Treated with Stent-Assisted Coil Embolization

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## ABSTRACT

**BACKGROUND AND PURPOSE:** This study is a homogeneous series of circumferential unruptured intracranial aneurysms with large necks treated with stent-assisted coil embolization. Our purpose was to demonstrate which value of packing density is required to produce a durable occlusion.

**MATERIALS AND METHODS:** We retrospectively evaluated all patients with unruptured intracranial aneurysms who were treated with stent-assisted coil embolization having late angiographic control between 2004 and 2014, in a single large cerebrovascular referral center. To calculate the packing density, aneurysm volume, and coil volume, we used an on-line system.

**RESULTS:** In 49 circumferential unruptured intracranial aneurysms treated with stent-assisted coil embolization, 38.7% ($n = 19$) had complete occlusion in the immediate control. Of those with incomplete occlusion, 80% ($n = 24$) progressed to complete occlusion in the late angiographic follow-up. At late angiographic control, 87.7% ($n = 43$) of aneurysms were completely occluded. All aneurysms with a packing density of ≥19% were completely occluded. Packing density was the only statistically significant predictor of complete occlusion. None of the aneurysms with complete occlusion at immediate control or at late angiographic control had recurrence.

**CONCLUSIONS:** In circumferential aneurysms treated with stent-assisted coil embolization, packing density is the main predictor of complete occlusion. In this type of aneurysm, a packing density of ≥19% was enough to reach complete occlusion; knowing this is important to avoid higher packing densities that have more risk.

**ABBREVIATIONS:** PD = packing density; SACE = stent-assisted coil embolization; UIA = unruptured intracranial aneurysm

Unruptured intracranial aneurysms (UIAs) are present in 3% of the adult population and are increasingly detected due to more frequent use of noninvasive angiographic diagnostic imaging.[1-3]

Endovascular coiling for the treatment of intracranial aneurysms was first introduced into clinical use in 1990, and since then, the greatest concern has been the high recanalization rate, recently estimated to be approximately 20%.[4,5] This occurs more often in large-neck aneurysms,[6] which are currently treated with stent-assisted coil embolization (SACE).

In unassisted coil embolization, higher packing density (PD) rates are correlated with lower recanalization rates.[7-10] It is likely that in SACE treatment, the packing density necessary to reach a stable complete occlusion is lower, but there is no homogeneous study to confirm that possibility, to our knowledge.

The purpose of this study was to demonstrate which value of PD is likely to produce durable occlusion in a homogeneous series of circumferential, large-neck UIAs treated with SACE in a single cerebrovascular referral center.

## MATERIALS AND METHODS

The study protocol was approved by a local institutional review board. This is a single-center retrospective review of our data bank from February 2004 to June 2014. Clinical and image records were independently reviewed by a member of the research team who did not participate in the treatment of any of the included patients. The patient demographics, treatment details and effects, results of follow-up, and complications were recorded.

All patients were treated under general anesthesia, and stent-assisted coiling was performed on a biplane Integris Allura FD20/30 angiographic system (Philips Healthcare, Best, the Netherlands). Regular techniques were used, including prior use of dual antiplatelet therapy.

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**Table 1: Relationship between the location and number of the aneurysms**

| Location | No. | % |
|---|---|---|
| Middle cerebral artery | 11 | 22.4% |
| Anterior communicating artery | 9 | 18.4% |
| Basilar artery | 5 | 10.2% |
| Posterior communicating artery | 5 | 10.2% |
| Bifurcation of the internal carotid artery | 5 | 10.2% |
| Internal carotid artery | 3 | 6.1% |
| Pericallosal artery | 2 | 4.1% |
| Others | 9 | 18.4% |
| Total | 49 | 100% |

From the 310 aneurysms in 271 patients treated with SACE, we selected 49 unruptured circumferential wide-neck aneurysms, not previously treated in 47 patients, with 3D reconstruction angiography before treatment and at least 1 late angiographic control. The mean time from the operation until the first follow-up was 7.0 months. Wide-neck aneurysms were defined as having at least 1 of the following criteria: neck size $\geq$ 4 mm, dome-to-neck ratio $<$ 1.5, or a cylindric neck.

To calculate the packing density, volume of aneurysms, and volume of coils, we used an on-line system available at www.angiocalc.com. This calculation was based on the shape and size of the aneurysm and on the type and size of the coils. All aneurysms treated with coils that did not have calculations based on this site were excluded.

Of the 47 patients, 15 were men, and 32, women. The mean age was 56.7 years. Of the 49 aneurysms, 32 had wide necks ($>$4 mm), 42 had unfavorable dome-to-neck ratios ($<$1.5 mm), 26 had wide necks and unfavorable dome-to-neck ratios, and 2 had cylindric necks.

The relationship between the location and number of aneurysms is shown in Table 1.

Aneurysm obliteration rates on the immediate control and first follow-up angiograms were classified as complete (100%); any opacity in the neck or sac of the aneurysm was considered incomplete obliteration.

In the late angiographic control, we evaluated the rate of progression from incomplete to complete occlusion and whether there was recurrence of an aneurysm with initial complete occlusion. We compared these data with the location of the aneurysm, the volume of the aneurysm and coils, the PD, and the type of stent used.

We used 4 types of stents: the Neuroform stent (Stryker Neurovascular, Kalamazoo, Michigan) in 35 procedures, the LEO stent (Balt Extrusion, Montmorency, France) in 16 procedures, the Enterprise stent (Codman & Shurtleff, Raynham, Massachusetts) in 2 procedures, and the Solitaire stent (Solitaire AB neurovascular remodeling device; Covidien, Irvine, California) in 1 procedure.

### *Statistical Analysis*

Statistical analysis was performed by using R statistical and computing software, Version 3.2.2 (http://www.r-project.org/). For the relationships between volume and packing and volume and incomplete occlusion, the Pearson correlation coefficient was calculated. To obtain the relationship among age, sex, aneurysm volume, packing density, and volume of coils and complete occlusion at 6-month follow-up, we used logistic regression. We also calculated the corresponding 95% confidence interval to verify the existence of the relationship. The relationships between a high percentage of PD and complete occlusion and between large aneurysms and incomplete occlusion were assessed with logistic regression analysis. $P$ values $<$ .05 indicated a significant difference.

## RESULTS

In the immediate control, complete occlusion occurred in 38.7% of aneurysms ($n$ = 19), and incomplete occlusion, in 61.2% aneurysms ($n$ = 30). However, of those who had incomplete occlusion, 80% ($n$ = 24) progressed to complete occlusion and the remaining 20% ($n$ = 6) had incomplete occlusion (Fig 1). At the late angiographic control, 43 aneurysms (87.7%) had complete occlusion. There was no aneurysm recurrence in the first follow-up for those aneurysms that were completely occluded in the immediate control.

The mean volume of the 49 aneurysms was 175.2 $mm^3$ (median, 329.7 $mm^3$; range, 4.2–4849.9 $mm^3$). The mean coil volume was 38.5 $mm^3$ (median, 54.7 $mm^3$; range, 1.5–396.3 $mm^3$), and the average PD was 37.9% (median, 28.6%; range, 2.8%–54.9%).

Above 19% of PD, all aneurysms were completely occluded, independent of their volume (Fig 2).

According to Fig 2, the aneurysms were subdivided into 2 groups on the basis of volume: A, $<$179.6 $mm^3$ ($n$ = 37); B, $>$179.6 $mm^3$. In group A, all aneurysms except 1 had complete occlusion, independent of their PD. The only aneurysm incompletely occluded in this group was one in which we could not deploy a necessary second coil due to the impossibility of recatheterizing the aneurysm sac after the first coil. In group B, complete occlusion was reached for all aneurysms with a PD of $>$19%. Aneurysms of $>$179.59 $mm^3$ had a larger diameter, between 7.0 and 7.8 mm.

The statistically significant correlation coefficient ($P < .05$) between aneurysm volume and PD was −0.42 (95% CI, −0.62 to −0.15; $P$ = .003), and the correlation between aneurysm volume and incomplete aneurysm occlusion was −0.44 (95% CI, 0.18–0.64; $P$ = .002). The correlation coefficient between coil volume and PD was 0.26 (95% CI, −0.50 to 0.02; $P$ = .071), which is not statistically significant. Large volumes of coils are used in large aneurysms, which tend to have lower PD.

A multivariate analysis with predictive factors of complete aneurysm obliteration, including age, aneurysm volume, PD, and volume of coils, showed that the only statistically significant predictive factor was PD (Table 2).

Procedure-related complications occurred in 3 patients (6.4%, 3/47). In 2 patients (4.1%, 2/49), there was thrombosis of the stent after its release; one was treated with an intravenous infusion of a loading dose of abciximab (ReoPro), and the other, with an intra-arterial injection of tirofiban (Aggrastat) and mechanical thrombolysis, with full opening of the parent vessel. Both had a transient deficit and full recovery in 3 and 4 days, respectively. One patient (2.1%, 1/47) had an asymptomatic vertebral artery dissection, and a stent was placed at the site of dissection. There was no neurologic deficit in any of the 3 patients at discharge.

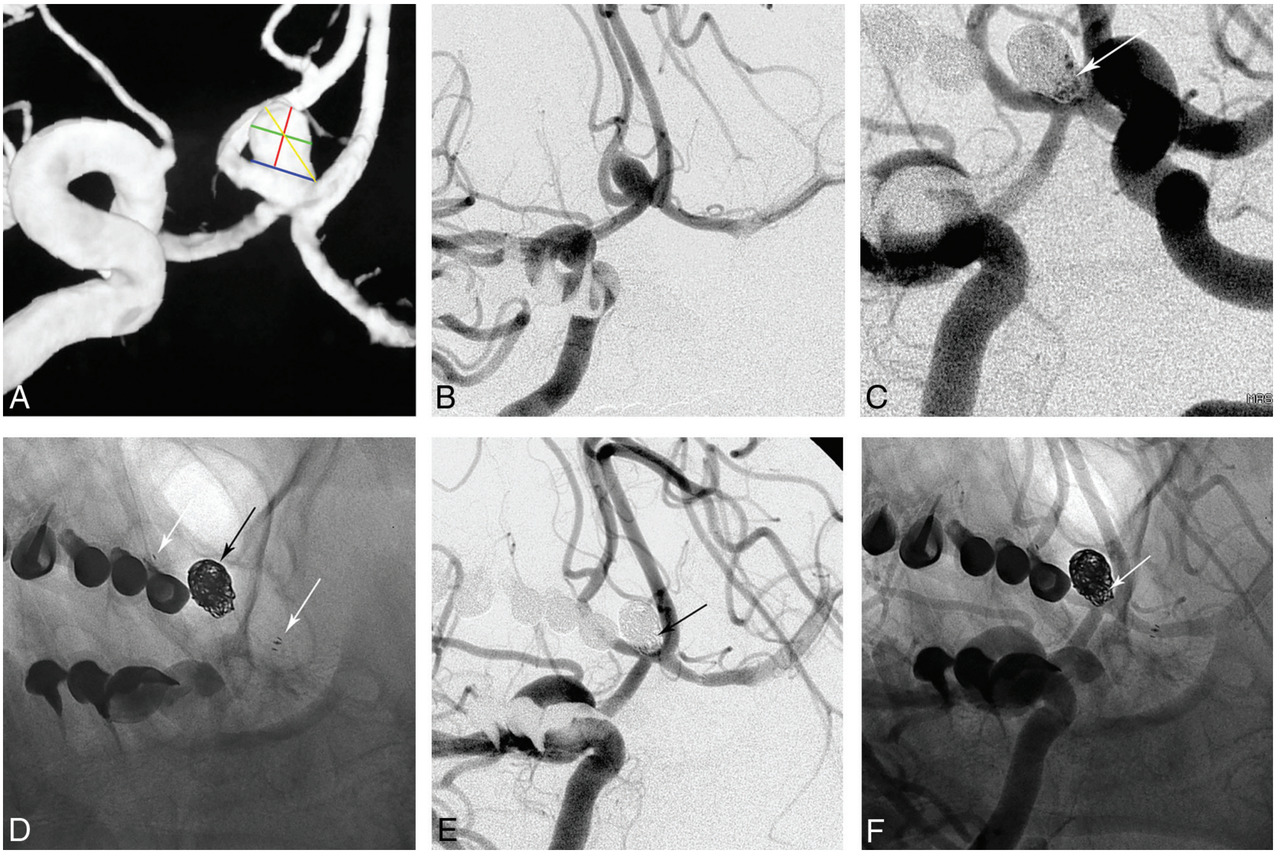


**FIG 1.** A 62-year-old man presenting with a small, incidental aneurysm of the anterior communicating artery. A 3D rotational angiogram (*A*) was obtained before the embolization. Measurements were made of the neck (*blue line*), diameter parallel to the neck (*green line*), height (*red line*), and largest diameter (*yellow line*). Projection work after a right internal carotid contrast injection (*B*) shows the relation of the anterior communicating artery aneurysm to the anterior cerebral arteries. Final control after simultaneous contrast injections in the internal carotid artery. *C* and *D*, Residual neck flow (*white arrow*) after stent-assisted coil embolization (stent, *white arrows*; coils, *black arrow*). Six-month angiographic controls (*E* and *F*) show the evolution to complete occlusion (*black* and *white arrows*).

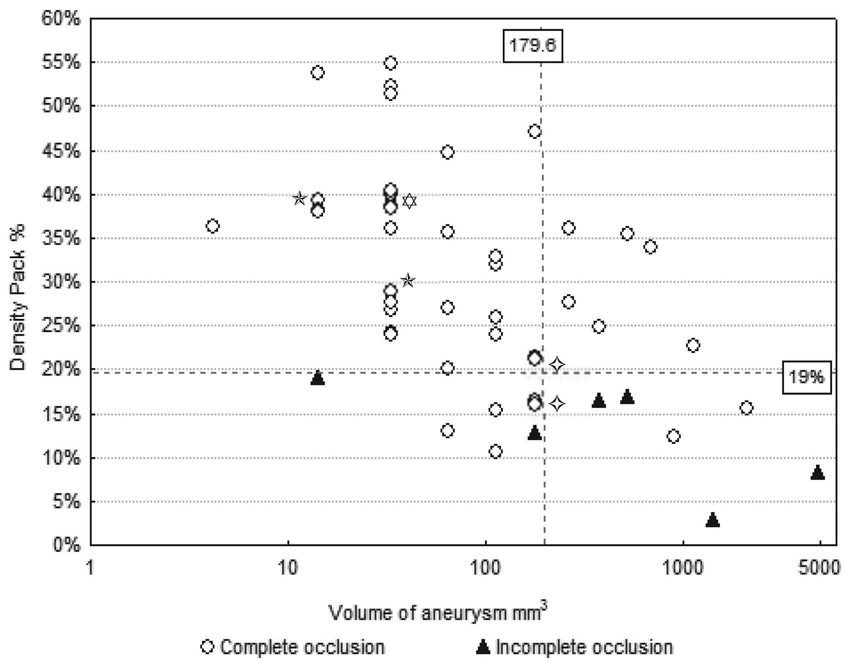


**FIG 2.** Results of the Pearson test, demonstrating that above 19% packing density, all aneurysms had complete occlusion. Regarding the volume, aneurysms above 179.6 mm$^3$ had a higher rate of incomplete occlusion when the packing density was below 19%. If >1 aneurysm is overlapping, note the following symbols: ✧, 2 aneurysms, ✯, 3 aneurysms, ✡, 4 aneurysms.

## DISCUSSION

Stent-assisted coil treatment for large-neck aneurysms has shown a higher rate of evolution to complete occlusion in the follow-up and a lower rate of late aneurysm recanalization compared with nonstented aneurysms.[6,8,11-14] The mechanisms involved are hemodynamic modification of the inflow angle to the sac, the presence of more metal on the neck, and the scaffold provided by the stent and coils favoring better endothelialization.[6,15-17] It is thought that the main predictor of immediate and late complete occlusion and the absence of aneurysm recurrence is the PD.[8,11,12,18-22]

However, we supposed that to achieve a higher PD, it is necessary to place several coils inside the aneurysm, increasing the treatment time, the risk of thromboembolic and hemorrhagic complications, and the cost of the procedure.

Gallas et al[23] found that 26% of aneurysms had an incomplete occlusion among 1036 aneurysms treated with coils.

**Table 2: Multivariate analysis of predictive factors for complete occlusion**

| | Relative Risk | 95% CI | *P* Value |
|---|---|---|---|
| Sex | 0.933 | 0.254–6.045 | .929 |
| Age | 0.746 | 0.089–2.345 | .684 |
| Volume of the aneurysm | 1.001 | 1.000–1.002 | .079 |
| Packing density[a] | 0.876 | 0.657–0.955 | .012 |
| Volume of the coils | 1.005 | 0.998–1.011 | .123 |

[a] Significance level is .05.

Raymond and Roy[7] reported that incomplete occlusion in the immediate control of aneurysms treated with coils is a risk factor for aneurysm recanalization. Piotin et al[11] reported that aneurysms treated with SACE had lower recanalization rates than nonstented aneurysms. Lawson et al[22] identified PD as a predictor of complete occlusion in aneurysms treated with SACE.

Chalouhi et al[8,13] found an adequate PD of 12%–22% for complete occlusion of aneurysms in angiographic follow-up tests in 290 aneurysms treated with SACE, but the aneurysm recurrence rate was not reported.

Unlike others, our study considered only circumferential saccular UIAs, homogenizing the group to find the PD required for a high complete aneurysm occlusion rate, with low rates of recurrence and complications during the procedure.

Our study presented a rate of 38.7% ($n = 19$) with complete occlusion and 61.2% ($n = 30$) with incomplete occlusion in the immediate control. Of those in the latter group, 80% ($n = 24$) progressed to complete occlusion in the late angiographic follow-up.

PD is the main predictor of complete occlusion and aneurysm recurrence. Our study found all aneurysms with PD ≥19% with initial incomplete occlusion evolved to complete occlusion in the late angiographic follow-ups, with a statistically significant relationship between the variable PD and the first follow-up, in agreement with the study of Chalouhi et al.[8] Aneurysms with low PD (<19%) tended to not evolve to complete occlusion. None of the aneurysms that were completely occluded had recurrence, emphasizing the relevance of the flow-remodeling theory in the use of stents.[6,15-17]

However, aneurysms with smaller (<100 $mm^3$) and moderate (100–1150.3 $mm^3$) volumes had high rates of complete occlusion (96% and 85%, respectively), compared with aneurysms with greater volume (>1150.3 $mm^3$), demonstrating that smaller aneurysm volume can reach a better PD value with higher complete occlusion rates than those of large aneurysms, as described in the literature.[5,6,9,11,12,18,24] There was no statistically significant relation between the volume and packing density of an aneurysm: The *P* value was .079 (statistical significance, $P < .05$), probably due to the low number of aneurysms.

Sluzewski et al[9] reported that all aneurysms with packing densities of >24% and a volume of <600 $mm^3$, treated with coil embolization, had complete occlusion. We found that all aneurysms with packing densities of ≥19% independent of their volume had complete occlusion. This finding shows that stents help neck endothelization, requiring fewer coils to reach complete occlusion.[17]

No patient with complete occlusion in our study needed retreatment, and our complication rate was 6%. All patients were discharged without neurologic deficits and none died.

A limitation of our study is its retrospective, no randomization design in a single center with a small sample due to the inclusion of only circumferential UIAs. Another limitation is the use of a variety of regular stents and coils.

Today with the advancement of technology, new stents with lower porosity or double layers (eg, LVIS Blue, Lvis, Lvis Jr; MicroVention, Tustin, California) may produce different results, needing specific studies.

## CONCLUSIONS

This study shows that the SACE technique has high rates of evolution from incomplete-to-complete occlusion of aneurysms, without recurrence. The PD is the main predictor for complete aneurysm occlusion. All aneurysms with PD of ≥19% achieved complete occlusion. For small aneurysms, the rate of complete occlusion was higher than in large aneurysms because it is difficult to achieve an optimal packing density in large aneurysms. The PD needed to occlude large-neck aneurysms treated with stents is lower than in those without stents.

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