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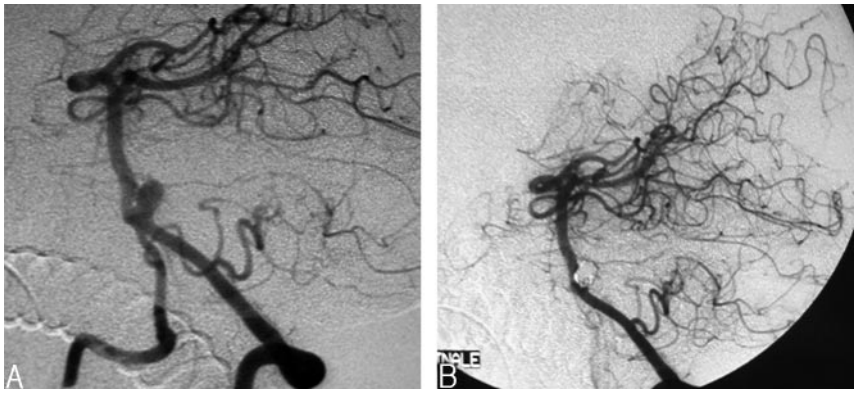

Fig 1. *A* and *B,* Pretreatment angiograms demonstrating saccular basilar artery aneurysm.

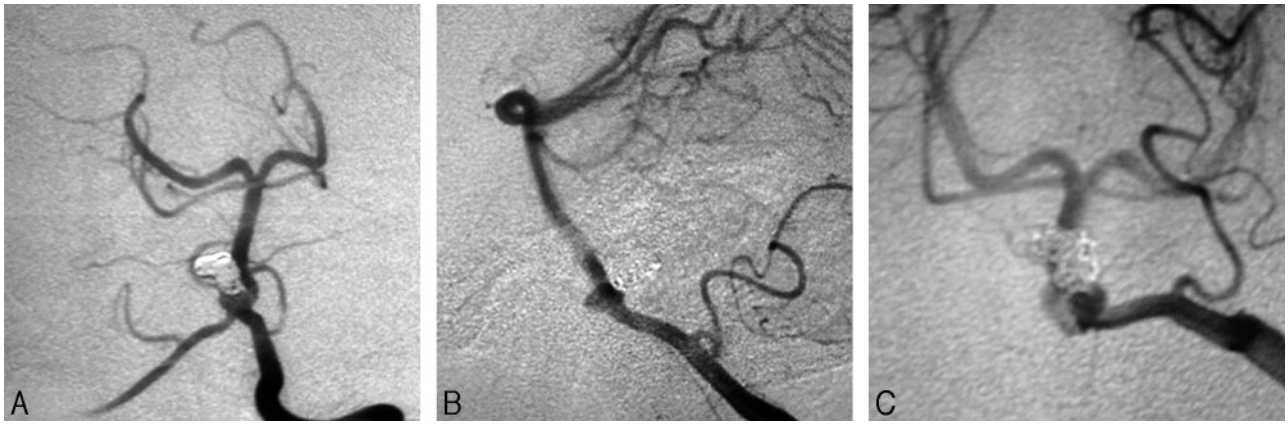

Fig 2. *A–C,* Posttreatment (with GDC and stent) angiograms of the de novo left vertebral-basilar junction aneurysm.

most significant allelic association, observed in *COL1A2* overexpression, results in an alanine to proline amino acid substitution, determines stability change in collagen I, and may affect the rigidity or elasticity of the vascular wall, causing aneurysm formation. In our opinion, significant vascular fragility may have occurred in our patient with phenotypically mild collagen disease, as confirmed by the association between the functional variant SNP28 and familial IA in a Japanese study.[4]

References

1. Albayram S, Kizilkilic O, Yilmaz H, et al. **Abnormalities in the cerebral arterial system in osteogenesis imperfecta.** *AJNR Am J Neuroradiol* 2003;24:748–50
2. Narvaez J, Narvaez JA, Majos C, et al. **Subarachnoid haemorrhage secondary to ruptured cerebral aneurysm in a patient with osteogenesis imperfecta.** *Br J Rheumatol* 1996;35:1332–33
3. Okamura T, Yamamoto M, Ohta K, et al. **A case of ruptured cerebral aneurysm associated with fenestrated vertebral artery in osteogenesis imperfecta** [in Japanese]. *No Shinkei Geka* 1995;23:451–55.
4. Yoneyama T, Kasuya H, Onda H, et al. **Collagen type I α2 (COL1A2) is susceptible gene for intracranial aneurysms.** *Stroke* 2004;35:443–48. Epub 2004 Jan 22

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Recently, the first results of a prospective multicenter registry in France using Matrix detachable coils (Boston Scientific, Natick, Mass) were reported in this journal.[1] We have serious concerns about the scientific validity of the reported results because of considerable inclusion and exclusion biases related to patients and aneurysms.

First, the authors presented 2 exclusion criteria for the registry: patients with a Glasgow Coma Scale score of <10 and patients with giant aneurysms "because the final goal of the registry was to evaluate the long-term anatomic results after endovascular treatment with Matrix detachable coils."

Exclusion of patients with bad clinical scores is likely to increase the angiographic follow-up rate but introduces several biases. For instance, a substantial proportion of patients with bad scores may have an intraparenchymal hematoma. Patients with intraparenchymal hematomas are at risk for early rebleeding after coiling of the ruptured aneurysm. In a study concerning the occurrence of early rebleeding after coiling, patients with a Hunt and Hess (HH) scale grade of III–V had a ninefold increased risk for early rebleeding compared with patients with HH I-II.[2] In the first registry concerning the use of Matrix coils (ACTIVE Study), an unacceptably high proportion of early rebleedings after coiling (7%) was noted.[3, 4] This study has not been published. Therefore, the concern of early rebleeding after coiling, especially with Matrix coils, is not eliminated by this registry, and the finding of the authors that no early rebleedings occurred is without meaning.

The second exclusion criterion is patients with giant aneurysms. If patients with giants aneurysms are excluded from long-term follow-

up, long-term durability will improve dramatically because most giant aneurysms that are coiled will show compaction at follow-up, necessitating retreatment.[5] Therefore, this exclusion criterion introduces an enormous bias toward better angiographic results on follow-up.

Moreover, on further reading, we realize that exclusion bias is not limited to patients with bad scores and giant aneurysms: in a 10-month period, 236 patients with 244 aneurysms were included from 16 centers from major cities in France. This means that on average, 15 patients per center were enrolled in the registry. We assume that most of these centers from major cities in France are large-volume centers; therefore, a considerable (but unknown) number of patients were additionally excluded for unknown reasons. On closer inspection of the data, 205 of 244 aneurysms (84%) were small and 198 aneurysms (81%) had a small neck. Apparently, an important inclusion bias existed in favor of small aneurysms with small necks. In many studies referred to in the article, it has been shown that results of coiling are most favorable in these small aneurysms with a small neck.

When the authors state, "Because selection for treatment with PGLA-coated coils or bare platinum coils was determined and performed by the treating neuroradiologist in each center, it is not possible to know whether a selection bias existed," they probably mean that they did not bother to look for any.

Any comparison of the results of this registry (sponsored by the manufacturer of the coils and written by a consultant of this company) with other studies is invalid because of the unacceptable inclusion and exclusion biases. In patients with good scores with small aneurysms with small necks, any type of coil will give satisfying results.

References

1. Pierot L, Bonafé A, Bracard S, et al, for the French Matrix Registry Investigators. **Endovascular treatment of intracranial aneurysms with Matrix detachable coils: immediate posttreatment results from a prospective multicenter registry.** *AJNR Am J Neuroradiol* 2006;27:1693–99
2. Sluzewski M, van Rooij WJ. **Early rebleeding after coiling of ruptured cerebral aneurysms: incidence, morbidity, and risk factors.** *AJNR Am J Neuroradiol* 2005;26:1739–43
3. Sluzewski M, van Rooij WJ. **Questionable interpretation of results of ACTIVE study on matrix coils by Boston Scientific.** *AJNR Am J Neuroradiol* 2005;26:2163–64
4. Sluzewski M, van Rooij WJ. **Reply to letter regarding interpretation of results of ACTIVE Study.** *AJNR Am J Neuroradiol* 2005;26:2436–37
5. Sluzewski M, Menovsky T, van Rooij WJ, et al. **Coiling of very large or giant cerebral aneurysms: long-term clinical and serial angiographic results.** *AJNR Am J Neuroradiol* 2003;24:257–62

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Reply:

We welcome the letter of van Rooij and Sluzewski regarding our article, "Endovascular Treatment of Intracranial Aneurysms with Matrix Detachable Coils: Immediate Post-Treatment Results from a Prospective Multicenter Registry."[1] We also thank the editor of the *American Journal of Neuroradiology* for giving us the opportunity to respond to his comments.

As indicated in our article, one of the primary goals of this study was to evaluate the long-term efficacy of the polyglycolic/polylactic acid–coated coils in the treatment of intracranial aneurysms. Therefore, patients with a Glasgow Coma Scale score of <10 were excluded to maximize the long-term follow-up rate of included patients. Indeed, this exclusion criterion introduces a bias regarding the overall morbidity-mortality rate of the series. That is the reason we did not compare the global morbidity-mortality rate of our series with that of other series in the literature. This being said, we believe that it is not clear from the literature that the frequency of adverse events is related to the initial severity of the clinical presentation. So in the perspective of assessing treatment-related complications, exclusion of patients in poor clinical condition represents a limited selection bias, and the comparison with other series in the literature is valid. Moreover, in most of these series, low scores were frequently excluded. Additionally, there is no evidence in the existing literature of a correlation between the initial clinical score and the long-term anatomic results. Thus, exclusion of patients with low scores is also not a methodologic bias for the long-term results.

van Rooij and Sluzewski write that "the finding of the authors that no early rebleedings occurred is without meaning." No early rebleeding was observed for the 138 included patients presenting with subarachnoid hemorrhage and treated with Matrix detachable coils (Boston Scientific, Natick, Mass). Additionally, recently analyzed 1-year clinical follow-up data also show no rebleeding at 1 year in our series. Because of the characteristics of our population, the question of early rebleeding after coiling of ruptured intracranial aneurysms with Matrix coils is not completely resolved by our results. Moreover a comparative series is probably needed to answer the question of the comparative risk of early rebleeding after treatment with Guglielmi detachable coils (GDC) or Matrix coils. However, the fact that no early or midterm rebleeding was observed in our series remains meaningful and indicates that this risk is low.

The reality of intracranial aneurysms is complex and heterogeneous. One encounters several types: fusiform, sacciform, small, large, giant, dissecting, and associated with a brain arteriovenous malformation (AVM). Treatment strategies and expected results are certainly different for these diverse groups. Because our goal was to evaluate the selective endovascular treatment of aneurysms with Matrix coils in a homogeneous population, fusiform, dissecting, AVM-associated, and giant aneurysms were excluded. In that perspective, one needs to keep in mind that according to the largest series in the literature, the percentage of giant aneurysms is very low (2% in the International Cooperative Study[2]) and inclusion of giant aneurysms in our series would probably not have significantly modified our findings regarding immediate clinical and anatomic results, which are the topics of the present article.

Patients were not consecutively included in our registry, and this is probably a methodologic weakness. However, it is certainly not possible to say that "an important inclusion bias existed in favor of small aneurysms." In fact, the percentage of small aneurysms reported in our series is in the range of the largest series of the literature: 78% in the International Cooperative Study on the Timing of Aneurysm Surgery[2] and 94.7% in the largest endovascular series.[3] With regard to the size of the neck, one cannot state that a bias existed in our series. There are, indeed, several ways to classify the size of the neck. We used the classification proposed by Vinuela et al,[4] but we all know that the absolute value of the size of the neck is probably less meaningful than the dome-to-neck ratio. In our series, this ratio was <2 in 57% of the aneurysms. Finally, most series do not report the size of the neck of the aneurysm treated, and in that perspective, it is not possible to know whether our series is different from others.

Our article presents the first prospective multicentric evaluation of the Matrix coils in the selective endovascular treatment of intracra-