

Despite the use of DMT in 94% of patients with a relapsing remitting course (Table), they had experienced a higher than expected relapse rate of 0.9/year. However, the patients in our population had MS associated with CCSVI. For this peculiar association, we measured in our pilot study if angioplasty treatment of CCSVI could modify the neurologic outcome of MS.

The endovascular treatment, despite the 47% restenosis rate recorded in the internal jugular veins, reduced, although not significantly, the annualized relapse rate from 0.9 to 0.7. Relapse did recur in 50% of patients compared with 77% registered in the previous 2 years ($P = .0014$). As stated in the article, relapses as well as new T1 gadolinium-positive lesions did not occur in patients with patency of the major cerebral veins: two objectively measured facts and not a sham effect. Actually, we are conducting long-term follow-up of the same cohort.

We think it would be highly irresponsible to not report to colleagues such preliminary results. The excitement is understandable for patients and is linked to two reasons. The first is the awareness that MS, ranging from 56% to 100% of cases, can be associated with a major vascular problem.^{2,4-6} The second is that the latter may have a resolution through a minimally invasive surgery.

Knowing if this is a sham or a real therapeutic effect for MS is a precise responsibility of the medical community, and not an opinion expressed in a scientific letter. As stated on page 1357 line 35, a randomized, controlled, double-blind study is the only tool that can answer the question of Dr Requarth. This will start in the next months involving several centers in Italy.

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Regarding "A prospective open-label study of endovascular treatment of chronic cerebrospinal venous insufficiency"

In the article "A prospective open-label study of endovascular treatment of chronic cerebrospinal venous insufficiency," by Zamboni et al,¹ the authors compared pre- and post-therapy outcomes with two-sample statistical analyses as though the outcomes arose from independent groups of patients (page 1351 of the article). They did not present within-patient results or use paired statistical tests for change in venous pressure or neurologic outcomes. Their reported use of Fisher exact test to analyze annualized relapse rates is not appropriate because those data are not proportions or numbers of patients. Tables IV and V fail to state the number of patients included in these results. One might suspect that not all 35 relapsing remitting patients contribute to Table IV, as no counts yield percentages of 27% (9: 26%, 10: 29%) or 50% (17: 49%, 18: 51%), for example.

Given the attention that Dr Zamboni's results have received, the reader would welcome an addendum with clarification and information that is more complete. It is possible that the appropriate paired testing would provide similar or greater degrees of statistical significance, bolstering hope for the effectiveness of percutaneous transluminal angioplasty in treating multiple sclerosis patients.

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Reply

Our study is a pilot study with promising results. It shows two main shortcomings: the lack of a control group and blinded clinical assessors. We chose to use statistical tests to underestimate rather than exalt our findings, precisely because of the above limitations. The tests suggested by you, as you noted at the end of your letter, provide even greater degrees of statistical significance. Our policy is to be as prudent as we can, waiting for randomized control trial angioplasty results. The main message of our study is the safety and the feasibility of venous angioplasty in patients affected by chronic cerebrospinal venous insufficiency associated with multiple sclerosis (CCSVI-MS).¹

However, differences in quality of life and multiple sclerosis functional composite among neurologic outcomes were re-assessed also with paired t test, as you requested in your letter, and were significantly different. For instance, MSFC in relapsing remitting patients by comparing baseline with 18 months value showed a highly significant improvement of the motor and cognitive function expressed by such functional composite test ($P < .0001$).

Differences in preoperative and postoperative pressure were assessed with the two-tailed Mann-Whitney test, as reported at page 1351 of our article.¹