Reply to letter regarding article titled 'Microembolism during foam sclerotherapy of varicose veins' in the *New England Journal of Medicine*

We regret that the *New England Journal of Medicine* (*NEJM*) did not give the opportunity to publish Simka's commentary on our letter published in the 3 April 2008 issue of the *NEJM*.[1] Indeed, our letter seems to have a major impact proven as being the most blogged paper published in the *NEJM* this year. Given Simka's commentary, we would like to respond since our paper might have caused some discomfort among others.

To the best of our knowledge, our paper is the first published study investigating the systemic distribution of foam during foam sclerotherapy (FS) after experiencing neurological symptoms during FS in two patients. FS was carried out following the European consensus guidelines.[2] We demonstrated that a common event in all patients undergoing FS is the presence of foam microembolism, or 'small echogenic structures' as suggested by the consensus meeting 2006. In a significant number of patients, a patent foramen ovale (PFO) was present resulting in microembolism in the left side of the heart. Also, in our two index patients, further examination revealed a PFO. From these observations, we concluded that microembolism induced by FS potentially cause neurological symptoms in the presence of a PFO.

Although no scientific evidence is available so far, we are convinced that the injection of foam prepared by mixing polidocanol with room air results in air embolism with active sclerosant coating.

The occurence of neurological symptoms in patients with PFO is probably related to the total amount of microembolism in the left side of the heart and is subsequently PFO size dependent. It is surprising that none of the five patients with a PFO described in our study developed neurological symptoms. However, we neither quantified the amount of microembolism in the left side of the heart nor the size of the PFO in these patients.

In accordance with our data, Regan *et al.*[3] report that embolism after FS was detected in the medial cerebral artery in 90% of the patients with a PFO. None of these patients developed neurological symptoms. Interestingly, Regan did not use room air for the production of foam, but applied the Varisolve-technique using a low-nitrogen gas mixture resulting in smaller bubble size and higher rate of reabsorption.[3,4]

In conclusion, we fully agree that the incidence of neurological symptoms following FS is very low.[5] Nevertheless, we believe that caution should be exercized when FS is performed. Patients developing overt neurological complaints after FS should receive an additional echocardiographic examination to search for a PFO. Further research is needed to determine whether foam microembolism can cause cerebral micro-infarction independently of the presence of neurological complaints. Further evaluation of the different foam preparation techniques and different foam characteristics in relationship to the possible negative effects of these gas embolism are necessary.

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