Response to Letter by Vernooij et al

Response:
We thank Vernooij et al for their interest in the BRASIL study and for giving us the opportunity to explain our interpretation of the data. Vernooij et al conclude that BRASIL is compatible with a “substantial increased risk” of hemorrhage associated with thrombolysis therapy in patients with cerebral microbleeds (CMBs). We agree. It is stated explicitly in the article that the data are compatible with an increase in hemorrhage risk. However, it is essential that any such risk is set against the benefit of thrombolysis. What Vernooij et al mean by “substantial” is unclear in this respect.

Clinicians need to make treatment decisions based on the absolute likelihood of benefit for individual patients and trial results should be expressed as absolute risk reductions. Based on a large pooled analysis of randomized trials of thrombolysis in acute ischemic stroke the absolute reduction in the rate of hemorrhage was estimated to be 13% (95% CI: 4% to 22%) in CT-selected patients, and the benefit might be even higher if selection is based on MRI. The results of BRASIL suggest that the presumed CMB related excess absolute risk of hemorrhage is unlikely to exceed this absolute benefit of thrombolytic treatment.

The BRASIL data were collected by 13 experienced high-volume stroke centers with an overall detection rate of CMBs typical for MRI in acute stroke. Although this approach results in a high external validity for acute stroke imaging, there is certainly room for improvement of MRI techniques. We agree that a large prospective study with standardized MRI parameters would allow a more precise estimation of the CMB related risk. It is well established that even small differences in imaging techniques influence size and number of CMBs. The higher CMB rate in the general population of ischemic stroke patients might be explained by higher image quality in epidemiological studies where MRI is less time critical. Differentiating amyloid angiopathy from hypertensive angiopathy based on a CMB pattern is not very promising in the BRASIL dataset as the number of CMBs in the individual patients is low.

For the time being, we need to make decisions for or against the thrombolytic therapy which has been proven highly effective by several independent trials. Withholding this therapy needs a strong rationale. Such a rationale is not given by BRASIL.

Disclosures
None.

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