Response to Letter Regarding Article  
“Endothelial Activation in Lacunar Stroke Subtypes”

Response:  
We thank Dr Tsuda for his comments on our article in the August 2010 issue of Stroke regarding the hemostasis-related endothelial markers in first-ever lacunar stroke patients.1  
First, Dr Tsuda points to the relation between the endogenous nitric oxide inhibitor asymmetrical dimethylarginine and cerebral small vessel disease, in particular in relation with ischemic white matter lesions.2 In our study, we evaluated endothelial function by measuring levels of hemostasis-related proteins normally excreted by the endothelium, and did not measure levels of asymmetrical dimethylarginine. The increased levels of asymmetrical dimethylarginine found by Khan et al are in line with our findings of elevated levels of hemostasis-related markers, both suggesting that endothelial dysfunction is of importance in cerebral small vessel disease.  

Second, Dr Tsuda cites several studies in which the association between high levels of asymmetrical dimethylarginine, inhibiting nitric oxide, and blood pressure levels are evaluated. Hypertension is an important risk factor for cerebral small vessel disease.3 The relationship between blood pressure and endothelial function is quite complex. Increased blood pressure may be one of the factors that induces injury to the endothelial layer and causes endothelial dysfunction. Conversely, the vasomotor function of the endothelium regulates blood pressure, and endothelial dysfunction could thereby increase blood pressure. Therefore, finding an association between hypertension and increased levels of markers of endothelial function might be of interest. However, such an association will not tell us which factor is causative and which is consecutive. Furthermore, we suggest that future studies should use ambulatory 24-hour blood pressure levels instead of the dichotomous defined variable of hypertension.4  
We believe that evaluating the complex relationship between these blood pressure characteristics and different markers of endothelial function in cerebral small vessel disease is an interesting suggestion for additional research.

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