Response to Letter by Tsuda

Response:

We thank Dr Tsuda for his comments on our article demonstrating an association between the endogenous nitric oxide synthase inhibitor, asymmetric dimethylarginine (ADMA), and cerebral small vessel disease (SVD), and a correlation between ADMA and leukoariosis severity.1 We proposed that this association may be consistent with a role for endothelial dysfunction in the pathogenesis of SVD with smaller perforating artery damage resulting in leukoariosis.

There is a strong association between hypertension and SVD, especially in the presence of confluent leukoariosis.2 An association between ADMA and hypertension has also been suggested.3 The hypothesis suggested by Dr Tsuda that SVD patients with elevated ADMA have hypertension-induced endothelial dysfunction is attractive. In our study, SVD patients and controls were matched for hypertension defined categorically as systolic blood pressure $\geq 140$ mm Hg or diastolic blood pressure $\geq 90$ mm Hg or current treatment with antihypertensive drugs. In SVD patients, there was no correlation between systolic blood pressure ($R = -0.062$, $P = 0.681$), diastolic blood pressure ($R = -0.269$, $P = 0.068$), mean arterial blood pressure ($R = -0.187$, $P = 0.208$) and ADMA. Furthermore, no correlation between systolic ($R = 0.233$, $P = 0.115$), diastolic ($R = 0.153$, $P = 0.306$), mean arterial pressure ($R = 0.201$, $P = 0.157$), and leukoariosis grade was seen. In controls, no correlation was seen between systolic ($R = 0.279$, $P = 0.105$), diastolic ($R = 0.016$, $P = 0.928$), and mean arterial blood pressures ($R = 0.156$, $P = 0.369$) and ADMA.

Several factors may contribute to the lack of correlation between blood pressure and ADMA and between blood pressure and leukoariosis grade in our study. First, the sample size in this study is small and underpowered to detect the tested associations. Second, 36 out of 37 hypertensive SVD patients (97%) were using antihypertensive medications, as were 12 out of 30 hypertensive controls (40%). Therefore, using blood pressure readings at one point in time to establish the severity of hypertension is likely to be a very poor measure of longer-term hypertension. Finally, antihypertensive medication may additionally have an effect on ADMA levels.4,5

Disclosures

None.

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