

The Nerve! Readers Speak

Reader response: Prevalence of and risk factors for cerebral microbleeds in a general Japanese elderly community

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We thank Yubi et al.¹ for their study, which reports an intriguing result—a significant association between hypertension and lobar cerebral microbleeds (CMBs). Our concern is as follows: hypertensive arteriopathy is generally associated with nonlobar CMBs.^{2,3} Systemic hypertension is also thought to have a role in the pathology of mixed (lobar and deep/infratentorial) CMBs.² Furthermore, current knowledge suggests that hypertension concurrently with cerebral amyloid angiopathy (CAA) synergistically contributes to lobar CMB development.⁴ However, it is unclear in this prospective cohort¹ if the significant association of hypertension with lobar microbleeds is in fact with inclusive lobar microbleeds (those with both lobar and nonlobar CMBs) or exclusive lobar microbleeds (only lobar without nonlobar CMBs). If the former, then it is possible that the association is merely a statistical contribution of the deep/infratentorial CMBs included in the group, also taking into consideration the mean older age group and the undiagnosed CAA burden in the aging population. If the latter, it sheds light on an exciting new course for future neuropathologic and topographic studies in patients with CMBs.

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4. Cordonnier C, van der Flier WM. Brain microbleeds and Alzheimer's disease: innocent observation or key player? *Brain* 2011;134:335–344.

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We thank Dr. Vilanilam and colleagues for the comment on our article.¹ Our cross-sectional study showed a significant association of hypertension with not only deep/infratentorial cerebral microbleeds (CMBs) but also lobar CMBs. Among the 123 patients with lobar CMBs, 67 had microbleeds in cerebral lobes only (strictly lobar CMBs) and 56 had microbleeds in both lobar and deep/infratentorial regions (mixed CMBs). In Table 5 of the original article,¹ the multivariable-adjusted odds ratio (OR) of hypertension for the presence of lobar CMBs was 1.89 (95% confidence interval [CI] 1.09–3.28; $p = 0.02$). Since this analysis did not distinguish mixed CMBs from lobar CMBs, we performed the sensitivity analysis for strictly lobar CMBs, defined as lobar CMBs without deep/infratentorial CMBs, and observed a similar association (OR 2.12; 95% CI 1.00–4.50; $p = 0.04$) (table e-1, links.lww.com/CPJ/A24).¹ Our findings suggest that hypertension contributes to the development of lobar CMBs regardless of the presence of deep/infratentorial CMBs. Cerebral amyloid angiopathy (a major cause of lobar CMBs) and hypertensive angiopathy may coexist in lobar CMBs.² In addition, hypertension and cerebral amyloid angiopathy are likely to

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contribute synergistically to the development of lobar CMBs.³ Further neuropathologic and experimental studies are necessary to clarify the pathologic mechanisms for the development of lobar CMBs.

1. Yubi T, Hata J, Ohara T, et al. Prevalence of and risk factors for cerebral microbleeds in a general Japanese elderly community. *Neurol Clin Pract* 2018;8:223–231.
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3. Cordonnier C, van der Flier WM. Brain microbleeds and Alzheimer's disease: innocent observation or key player? *Brain* 2011;134:335–344.

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