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DOI: [10.1159/000355046](https://doi.org/10.1159/000355046)**Reply to the Comments by Prof. Yomoyuki Kawada**

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We are grateful to Prof. Tomoyuki Kawada for these statistical comments [1]. He suggested that there was no detailed description of the variable selection in the Cox proportional hazards regression model and the insufficient sample size precluded our study from constructing stable multivariable regression models to arrive at solid conclusions.

In the Cox proportional hazards regression model of our study, the confounder profile for subsequent intraventricular hemorrhage in moyamoya disease was selected from risk factors which had previously been reported or considered rational. They were simultaneously included for multivariate analysis. However, due to the limited events during the 23-month follow-up, it indeed could not reach the threshold of 10 events for each variable. It has been recognized as the major limitation of our study, which was fully addressed in the Discussion section on p. 474 [2].

We are totally aware that the optimal way to keep the statistical validity in multivariate analysis is to create a larger cohort [3]. However, as this is an uncommon disease, the incidence of moyamoya disease ranges from 0.02 to 0.41 per 100,000 people in Asia

[4]. It is extremely difficult to obtain large cohorts prospectively, especially based on susceptibility-weighted imaging, which is relatively new and has so far not been regularly performed in routine clinical practice [5]. Thus, as we have previously discussed [2], we may emphasize here again that due to the limited sample size, the conclusion that there is a relationship between intraventricular hemorrhage and cerebral microbleeds should be regarded with caution and is not suggested to be used as the basis for clinical practice without further confirmatory studies.

References

- 1 Kawada T: Risk assessment for cerebral microbleeds and intraventricular hemorrhage in patients with moyamoya disease by multivariate analysis. *Cerebrovasc Dis* 2013;36:326.
- 2 Sun W, Yuan C, Liu W, Li Y, Huang Z, Zhu W, Li M, Xu G, Liu X: Asymptomatic cerebral microbleeds in adult patients with moyamoya disease: a prospective cohort study with 2 years of follow-up. *Cerebrovasc Dis* 2013;35:469–475.
- 3 Peduzzi P, Concato J, Feinstein AR, Holford TR: Importance of events per independent variable in proportional hazards regression analysis. II. Accuracy and precision of regression estimates. *J Clin Epidemiol* 1995; 48:1503–1510.
- 4 Kleinloog R, Regli L, Rinkel GJ, Klijn CJ: Regional differences in incidence and patient characteristics of moyamoya disease: a systematic review. *J Neurol Neurosurg Psychiatry* 2012;83:531–536.
- 5 Baik SK, Choi W, Oh SJ, Park KP, Park MG, Yang TI, Jeong HW: Change in cortical vessel signs on susceptibility-weighted images after full recanalization in hyperacute ischemic stroke. *Cerebrovasc Dis* 2012;34: 206–212.