
Response:

We thank Plas et al1 for their interest in our article and for sharing their results about the smoking–thrombolysis paradox in ischemic stroke. A meta-analysis is an important further step to clarify the much debated and often conflicting results on this topic. Plas et al1 performed an analysis of 7 studies including 7494 patients receiving thrombolysis, which revealed an odds ratio of 1.38 (95% confidence interval, 1.24–1.53; \( P = 0.02 \)) for smoking in favor of a good functional outcome (modified Rankin Scale score \( \leq 2 \)) 3 months after stroke. The authors pointed out that the lack of adjustment for age and sex is a limitation of their analysis. This is an essential point, because smokers tend to be significantly younger and more often are men. Age is a strong predictor for outcome and studies have shown gender-specific differences in vascular risk factors and functional recovery.2 Nonetheless, the meta-analysis is reassuring that our observation is not a mere result of chance. An appropriately adjusted meta-analysis is without a doubt still necessary to determine the concrete effects of smoking on ischemic stroke.

Two recent studies have shed light on possible pathophysiological mechanisms underlying this peculiar phenomenon. One suggests smoking to have early protective effects and the other suggests an enhanced treatment efficacy in patients with this risk factor. Lisi et al3 provide evidence suggesting that short-term exposure to reactive oxygen species caused by smoking triggers ischemic preconditioning, reducing endothelial susceptibility to ischemia and reperfusion damage. Nielsen et al4 propose that smoking alters the nature of plasmin–antiplasmin–carbon monoxide interactions in blood plasma, consequently modifying fibrin clot kinetics. Earlier studies have demonstrated that smoking decreases endogenous tissue-type plasminogen activator release, causing an increase in fibrinogen levels and more fibrin-rich thrombi, thereby increasing susceptibility to exogenous tissue-type plasminogen activator treatment.5

Smoking remains a proven risk factor for stroke and has detrimental effects on the cardiovascular system. Whether smoking leads to increased tissue-type plasminogen activator efficacy deserves further studies. Either way, we continue to believe that no stroke is always better than a recanalized stroke.

Disclosures

None.

References

Response to Letter Regarding Article, "Smoking-Thrombolysis Paradox: Recanalization and Reperfusion Rates After Intravenous Tissue Plasminogen Activator in Smokers With Ischemic Stroke"

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