Letter by Dai et al Regarding Article, “Targeting Recombinant Tissue-Type Plasminogen Activator in Acute Ischemic Stroke Based on Risk of Intracranial Hemorrhage or Poor Functional Outcome: An Analysis of the Third International Stroke Trial”

To the Editor:

Whiteley et al demonstrated their excellent work to investigate the relationship among intravenous recombinant tissue-type plasminogen activator (rtPA), risk of symptomatic intracranial hemorrhage (sICH), and 6-month prognosis based on series of risk prediction scores. They drew the conclusion that there is a clinically relevant net positive effect of rtPA in patients with acute stroke at a high predicted risk of sICH or poor functional outcome, as it said in the abstract. However, we discuss some issues from statistical aspects.

In clinical practice, sICH remains the biggest concern when rtPA is administrated. sICH is associated with poor outcome after intravenous rtPA treatment, which is largely proved in previous articles. In the first paragraph of the Results section, it is listed that 8 of 104 sICH-positive patients (8%) were independent in activities of daily living at 6 months when compared with 546 of 1411 (39%) sICH-negative subjects (P<0.0001 by Pearson χ² test). However, to our surprise, based on Figure 2 in the article, rtPA showed even numeric greater absolute risk reduction in higher predicted risk of sICH group when compared with that in lower risk groups. The higher predicted risk of sICH, the more benefit derived from rtPA, is definitely not consistent with clinical observation. We think that there exists a possibility that the higher score-predicted risk of sICH group did not represent the high-risk group in the real situation.

In the article, the area under curve values of all selected models to predict sICH in rtPA-treated group (n=1515) ranged from 0.56 to 0.68, which was only moderately performed. On the basis of this score-predicted risk, they classified 1515 rtPA-treated patients as low, medium, and high risk with each model. In the last part of the Results section, to derive the absolute risk reduction values, another 1520 non–rtPA-treated patients were included in the analysis. This might suggest that these 1520 non–rtPA-treated patients were categorized based on each of those risk models as well, which raises a problem. These risk score models were derived to predict sICH risk of rtPA-treated patients. Whether they can be used in non–rtPA-treated patients needs to be further validated instead of directly applied because intravenous rtPA treatment may change the nature distribution of sICH events (rtPA may increase the risk of sICH by 5.8%) in patients with acute stroke.

As mentioned previously, these risk scores performed only moderately of rtPA-treated patients in International Stroke Trial-3. So if these risk scores need to be applied in non–rtPA-treated patients, we should first investigate how well did they perform in this cohort. We think that it would be more appropriate if the calibration and discrimination data in non–rtPA-treated patients are given in the article.

Disclosures

None.

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