Response to Letter by Prabhakaran and Lee

Response:

Drs Prabhakaran and Lee raise the important issue of mechanistic risk stratification in TIA. It is obviously desirable to enhance the accuracy of risk predictions after TIA using multiple clinical and imaging predictors. The CIP score intends to do this by incorporating simple clinical (the ABCD² score) and imaging information (DWI findings) often available to the physician after initial evaluation.¹ The clinical syndrome of TIA is a constellation of several etiologically heterogeneous conditions. The predictive value of prognostic TIA scores, including the CIP score, primarily depends on their ability to identify ischemia as the cause of symptoms. The diagnosis of ischemia is, however, a challenging task and often lacks a scientific foundation especially in patients with no acute ischemic lesion on DWI. Drs Prabhakaran and Lee argue that one should not conflate diagnostic scores with prognostic scores. It is not always possible to differentiate between diagnostic and prognostic scores in the setting of etiologically heterogeneous conditions; advanced diagnostic tests to further enhance the identification of an ischemic etiology will inherently convey some prognostic information in patients presenting with transient neurological symptoms.

Patients with positive DWI (also called transient symptoms with infarction or TSI),² on the other hand, represent a relatively homogenous subset caused by ischemia. Advanced diagnostic evaluation that directly relates to the vascular pathology and the mechanism of ischemia may enhance the accuracy of risk predictions in this subset. One challenge to developing advanced prognostic models in TSI is the selection of predictor variables. It has been suggested that predictor variables should be simple, powerful, affordable, prevalent, and reliable.³ Most candidate predictors for TSI do not quite meet these requirements. For instance, current MR-based perfusion-imaging techniques are associated with only moderate inter-rater reliability for detecting small ischemic regions observed in TSI.⁴ Another important barrier to reliable derivation of prognostic scores is the need for large sample size. Multivariable models used to develop prognostic scores are generally recommended to have more than 10 outcome events per predictor variable.⁵ The CIP was the largest published prognostic study of TIA with DWI (601 patients), yet despite this, there were only 23 outcome events. As a result, it included only the 2 most important variables, the ABCD² score and DWI. To construct a score, for instance, based on the 5 major etiologic stroke subtypes (with four degrees of freedom) will require more than twice the size of the CIP cohort. Moreover, practice changes as a result of recent evidence demonstrating that aggressive and rapid treatment of TIA can reduce the rate of subsequent stroke will further increase the number needed to generate an accurate prognostic model in the future.⁶ Developing reliable prognostic models that incorporate multiple clinical, imaging, and laboratory variables clearly requires a conjoint effort of multiple centers interested in the study of TIA.

Disclosures

None.

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