A Strong Start:
Plasma Glial Fibrillary Acidic Protein and Stroke Differential Diagnosis

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In the January issue of Clinical Chemistry, Foerch and colleagues (1) report on the diagnostic accuracy of plasma glial fibrillary acidic protein (GFAP)2 for differentiating intracerebral hemorrhage (ICH) and cerebral ischemia in patients with symptoms of acute stroke. This major, welcome effort from the Biomarker for Rapid Diagnosis of Hemispheric Stroke (BE FAST!) group cites highly significant differences in plasma GFAP collected within 4.5 h of symptom onset for acute stroke. No fewer than 14 centers (13 German and 1 Swiss) collected data on 205 patients during the 1-year period between June 1, 2009, and May 31, 2010. The diagnostic accuracy for ICH generated P values of <0.001, compared with ischemic stroke (IschSt) or stroke “mimic.”

A readily performed blood test that showed this large a difference would affect the management of acute stroke. It could spare the lost time and efforts of acute imaging tests to rule out ICH and speed the path to the use of thrombolytics or more-aggressive interventions. Granted the goal, this study has opened the door to more progress, but it leaves a number of major questions unsettled.

According to the described protocol, the immunoassay method for GFAP involves a 10-min centrifugation followed by two 9-min steps to prepare the sample for the Roche Elecsys analyzer (2), a rather large benchtop device. The authors noted in earlier publications (3, 4) that 2–6 h might be required for the evolution of the higher GFAP concentrations seen in ICH patients, thereby leading in the present study to a “lower diagnostic accuracy of the GFAP test in the very early phase of the disease (<2 h) as compared with the 2–6 h time window” (1). All told, the time needed for the current assay might approach the commonly applied limit for thrombolysis.

Clinicians would readily agree with the goal of having a point-of-care device that would provide rapid GFAP measurements for positively identifying patients with ICH in a prehospital setting. But where and in what prehospital setting would GFAP be measured? It is difficult to imagine performing these measurements in the typical frantic ambulance trip to a hospital. If the blood test can be performed only upon arrival at a hospital where the device is located, would not the time and effort involved in preparing and analyzing the blood sample be better used by conducting the medical-imaging examination that the a device would be designed to replace? We have no criticism of the effort in principle. One can hope that advances in techniques may yield the desirable goal of some device like a glucometer, which enables the measurement of blood glucose concentration via a finger stick.

The results from this effort had some curious omissions, the most notable being a lack of volumetric data for IschSt and no description of the imaging analyses performed for the ICH cases. A close inspection of the authors’ Fig. 3 reveals some major outliers in the IschSt group (1). Admittedly, Figs. 3A and 3B have huge differences in their ordinate scales, with none of the results for IschSt cases reaching the value of 1; however, 14 of the 37 ICH patients also had values <1, despite an increasing value for the group as a function of NIH Stroke Scale (and inferred increased volume). The authors themselves note that the GFAP test could miss cases of smaller ICHs, and this issue poses the biggest problem in diagnosis before imaging. Clinicians would be much happier to see the actual relationship to image volume and not just to the admission NIH Stroke Scale result (5). Might some of the highest GFAP values in the IschSt group have been hemorrhagic infarcts? Were the lowest GFAP values in the ICH group due to small ICHs in clinically sensitive regions such as the pons, or were they due to those individuals who were less symptomatic per volume for hemorrhages from arteriovenous malformations?

These comments and questions are intended not as criticisms but as evidence that clinicians evaluating these patients impatiently seek all the help they can receive.
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References


