Diagnostic value of serum versus plasma phospho-tau for Alzheimer’s disease

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Abstract

Background: Blood phosphorylated tau (p-tau) forms are promising Alzheimer’s disease (AD) biomarkers, but validation in matrices other than ethylenediaminetetraacetic acid (EDTA) plasma is limited. Firstly, we assessed the diagnostic potential of p-tau231 and p-tau181 in paired plasma and serum. Secondly, we compared serum and cerebrospinal fluid (CSF) samples from biomarker-positive AD and biomarker-negative control participants.

Method: We studied three independent cohorts (n=120 total): cohorts 1 and 2 included individuals with paired plasma and serum, while cohort-3 included paired serum and CSF. Blood-based p-tau231 and p-tau181 were measured using in-house or commercial Single molecule array (Simoa) methods.

Result: Serum and plasma p-tau231 and p-tau181 were two-fold increased in biomarker-positive AD versus biomarker-negative controls (P≤0.0008). Serum p-tau231 distinguished between diagnostic groups with area under the curve (AUC) of 82.2%-88.2% compared with 90.2% for plasma. Similarly, p-tau181 showed AUC of 89.6%-89.8% in serum versus 85.4% in plasma. P-tau231 and p-tau181 correlated slightly better in serum (rho=0.92-0.93) than in plasma (rho=0.88). Within-individual p-tau231 concentrations were twice higher in plasma versus serum, but p-tau181 levels were not statistically different despite a trend of higher concentrations in plasma. Bland-Altman plots revealed that the relative difference between serum/plasma was larger in the lower range. P-tau levels in paired plasma and serum correlated strongly with each other (rho=0.75-0.93) as well as with CSF Aβ42 (rho= -0.56 – -0.59), p-tau and total-tau (rho=0.53-0.73).
Conclusion: Comparable diagnostic performances and strong correlations between serum versus plasma pairs suggest that p-tau analyses can be expanded to research cohorts and hospital systems that prefer serum to other blood matrices. However, absolute biomarker concentrations may not be interchangeable, indicating that plasma and serum samples should be used independently. These results should be validated in independent cohorts.