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Letter to the Editor

Comparing Neurofilament Light Chain Levels in Serum and Plasma

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Dear editor,

Neurofilament light chain (NfL) has been suggested as a blood-based biomarker for neuroaxonal injury.[1] Blood level of NfL is known to be increased in diverse neurological disorders, including ischemic stroke, demyelinating disease, amyotrophic lateral sclerosis, frontotemporal dementia, and Alzheimer's disease.[2,3] Both serum and plasma NfL levels are associated with smaller hippocampal volume, thinner cerebral cortex, and longitudinal cognitive decline.[4,5] Depending on the study, serum or plasma NfL level was analyzed. Previous studies have reported a significant correlation between serum and plasma NfL levels.[6,7] However, it is unclear whether such correlation is well maintained under specific conditions such as old age and those who aer amyloid positive. Thus, the objective of this study was to investigate the association between serum and plasma NfL levels according to amyloid positivity.

Serum and plasma NfL levels of 38 participants (12 cognitively unimpaired, 18 mildly cognitively impaired, and 8 with dementia) were analyzed in this study. This study was approved by the Institutional Review Board of Hanyang University Guri Hospital (2018-01-015). Serum and plasma NFL levels were measured using an NF-Light Advantage assay (Quanterix, Boston, MA, USA, PN/103186) according to the Simoa Guide (Quanterix). Positron emission tomography scans were reviewed according to predefined regional cortical tracer uptake and brain amyloid plaque load (BAPL) scoring systems. A BAPL score of 1 was regarded as amyloid negative while BAPL scores of 2 and 3 were considered amyloid positive.[8] Wilcoxon's rank sum test was used to compare paired NfL data. Correlation between serum and plasma NfL levels was determined using Spearman's rho. All statistical analyses were performed using the Statistical Package for the Social Sciences for Windows version 21.0 (SPSS Inc., Armonk, NY, USA).

Of the 38 participants, 50% (n=19) were women. Their mean (± standard deviation) age was 70.6±9.5 years (range, 52 to 88 years). Amyloid positivity was observed in 16 (42.1%) participants. NfL levels were higher in the plasma (median: 29.6 pg/mL; 25% interquartile range [IQR]: 22.8–43.4 pg/mL) than in the serum (median: 27.7 pg/mL; IQR: 20.2–35.0 pg/mL, p<0.001). There was a strong correlation (Spearman's rho [r]=0.961) between serum and plasma NfL levels in the same participants (**Fig. 1A**). This strong correlation was consistently observed in female (r=0.956, n=19), male (r=0.960, n=19), amyloid-negative (r=0.975, n=22), and amyloid-positive (r=0.938, n=16) participants (**Fig. 1B-E**).

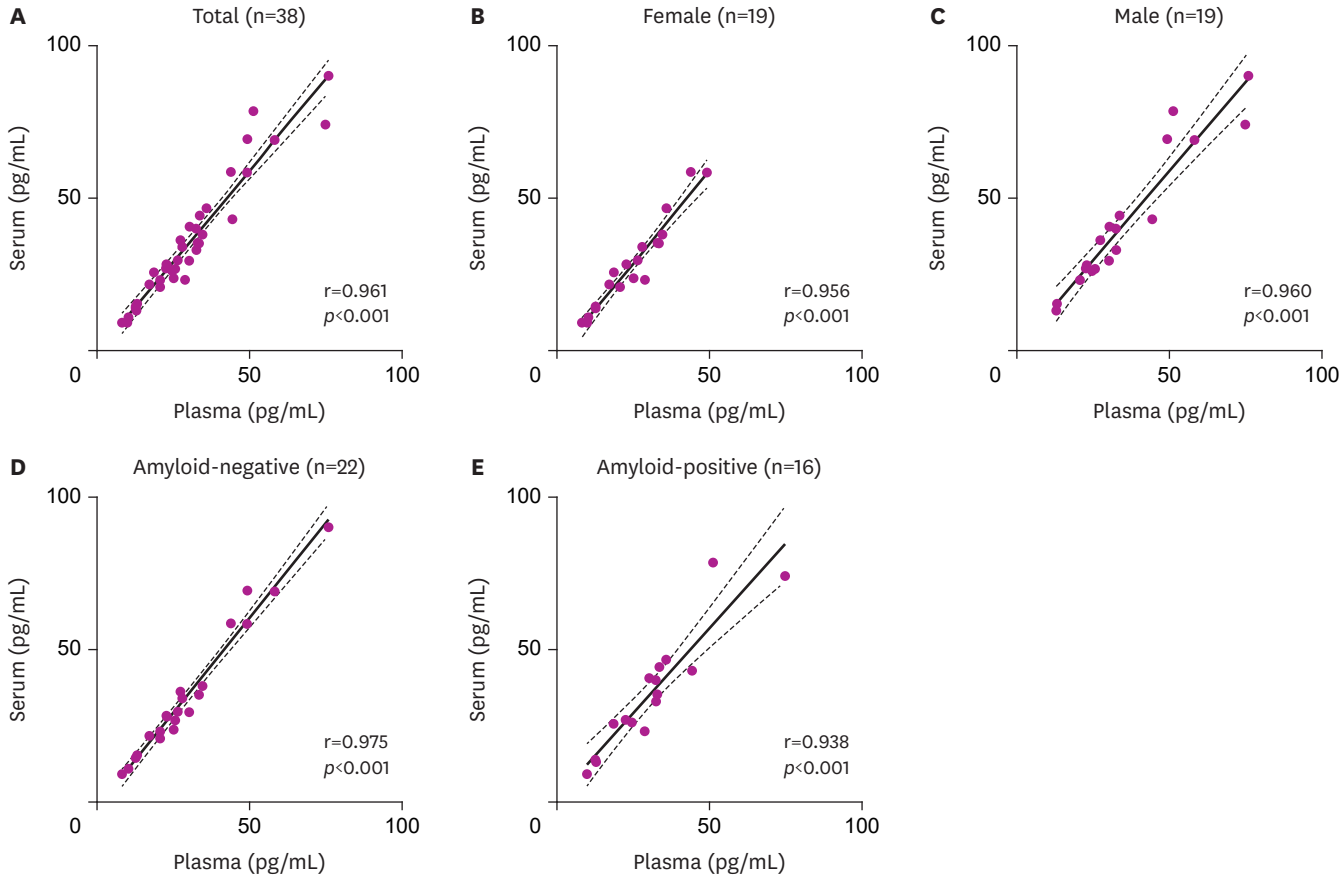

Fig. 1. Correlation between serum and plasma levels of neurofilament light chain in total (A), female (B), male (C), amyloid-negative (D), and amyloid-positive (E) participants.
r: Spearman's rho correlation coefficient.

Conflict of Interest

Seong-Ho Koh, Editor-in-Chief, and Hyuk Sung Kwon, Assistant Editor of *Dementia and Neurocognitive Disorders*, were not involved in editorial evaluations or the decision to publish this article. The authors have no conflicts of interest to declare.

Author Contributions

Conceptualization: Kwon HS, Koh SH; Data curation: Lee EH; Investigation: Lee H, Kim YS, Choi H, Lee KY, Lee YJ, Lee EH, Hwang M, Park H; Methodology: Kwon HS, Lee H, Lee EH, Hwang M, Park H; Supervision: Kim YS, Choi H, Lee KY, Lee YJ, Koh SH; Writing - original draft: Kwon HS; Writing - review & editing: Koh SH.

The strong correlation between serum and plasma levels is in line with previous reports analyzing healthy donors[9] or young patients with diverse neurological diseases (mostly multiple sclerosis).[6] However, the median level of NfL was significantly higher in the serum than in the plasma in two previous reports.[6,7] The reason for the difference between serum and plasma NfL levels is unclear. However, the current study showed that NfL levels in the serum were not always higher than those in the plasma. Additionally, the clinical significance of this difference might be low.[7] In conclusion, there is a strong correlation between serum and plasma NfL levels regardless of amyloid positivity or sex. Both serum and plasma NfL levels are expected to be useful biomarkers for diverse neurodegenerative diseases.

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